NUTRITIONAL MODULATIONS OF PIGLET GROWTH AND SURVIVAL

A Thesis

by

REZA REZAEI

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

December 2010

Major Subject: Nutrition

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Approved by:

Chair of Committee,	Guoyao Wu
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ABSTRACT

Nutritional Modulations of Piglet Growth and Survival.

(December 2010)

Reza Rezaei, DVM, Azad University, Garmsar, Iran

Chair of Advisory Committee: Dr. Guoyao Wu

This thesis research was conducted to test the hypothesis that the survival and growth of both neonatal and postweaning piglets can be improved by nutritional modulations. Two experiments were carried out to 1) evaluate effects of birth weight on mortality, growth performance, and efficiency of sow-reared piglets; and 2) determine the effects of a phytochemical (Yucca schidigera) on growth performance of postweaning pigs. In the first experiment, piglets (n=160) from 18 multiparous sows (Landrace ✕ Large White) were used. Body weight of all piglets were recorded immediately after birth, d 7, d 14, d 21 and d 35 of their age. Individual milk consumption of piglets was estimated using the weigh-suckle-weigh method. Average daily gain and mortality were recorded. To analyze the effects of birth weight on future BW and growth, piglets were classified based on their birth weight into four categories of A: 0.7-1.09 kg, B: 1.10-1.49 kg, C: 1.50-1.89 kg and D: >1.90. Data were statistically analyzed using one-way ANOVA. Results indicated that low birth weight of pigs not only increased ($P < 0.05$) their incidence of mortality but also negatively impacted ($P < 0.05$) their whole-body growth. Interestingly, surviving low-birth-weight piglets had a higher ($P < 0.05$) rate of efficiency to utilize milk nutrients for growth than larger littermates. In the second experiment, two 21-day trials using 21-d-old postweaning piglets (n=111) were performed (d 21 to 42 of age). In the first trial, pigs were assigned to one of the three groups fed diets supplemented with 0 (control), 120 ppm or 180 ppm of Yucca powder (BIOPOWDER). The second trial was conducted as the first trial except that the basal diet contained 0.2% L-citrulline (an effective precursor of arginine). Body weight, average daily gain and feed intake of all pigs were measured weekly in both trials. At the last day of experiment, 2 h after the last meal, jugular blood samples were taken from all pigs in both trials for amino acid analysis. One-way ANOVA was used to statistically analyze the data. When the basal diet did not contain citrulline, dietary supplementation with BIOPOWDER

did not affect ($P > 0.05$) any of the measured variables related to growth performance. However, supplementing an appropriate dose of this yucca extract (120 ppm) to a citrulline-fortified diet increased growth performance and feed efficiency in these animals. Adequate availability of arginine is required for BIOPOWDER to exert its anabolic effect on piglet growth and its regulatory action on improving the efficiency of nutrient utilization in young pigs. These findings have important implications for nutritionally modulating the growth of neonatal pigs and, therefore, the swine industry worldwide.

DEDICATION

I dedicate this thesis to my wonderful family, especially, to my father and mother for instilling the importance of hard work and higher education.

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It is a pleasure to thank those who made this thesis possible. I am heartily thankful to my supervisor, Dr Guoyao Wu whose encouragement, supervision and support from the preliminary to the concluding level enabled me to develop an understanding of the subject. He continually and convincingly conveyed a spirit of adventure in regard to research and scholarship and without his guidance and persistent help this thesis would not have been possible.

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INTRODUCTION AND LITERATURE REVIEW

INTRODUCTION

High neonatal mortality and suboptimal growth remain two major problems in the swine industry worldwide (Wu et al., 2006). These problems are particularly more severe for low-birth-weight piglets than normal-birth-weight littermates. A number of strategies have been used to improve the efficiency of pork production and they include new post-weaning feeding plans and dietary supplementation with functional amino acids (e.g., arginine and glutamine) (Wu et al., 2007, 2010a). However, these measures are used only for raising normal-birth-weight piglets and low-birth-weight piglets are usually culled from sows. Given a large number (25%) of pigs suffer from intrauterine growth retardation and their birth weights are less than 1.1 kg (Wu et al., 2006), much research is needed to enhance their preweaning and postweaning survival and growth.

The postweaning growth of pigs is closely related to their preweaning health status. While piglets are exposed to many stressors immediately after birth, gastrointestinal problems are among the most severe. The neonate instantly transits from primarily parenteral to enteral nutrition, which requires the small intestine to be the major organ for digestion and absorption of dietary nutrients. However, the gut of the neonatal pig is underdeveloped and highly susceptible to injury and oxidative stress. Thus, the main losses in pig production occur from birth to weaning. Most pre-weaning mortality in piglets takes place during the first 3 days after birth (Tuchscherer et al., 2000). In a study by Glastonbury (1976) the mean total mortality prior to weaning was 19.7% (n=10000 piglet), and most losses occurred during the first 4 days after birth. Based on another pre-weaning mortality study on pigs conducted by Svendsen et al. (1975) 2.8 % of the live-born pigs died with enteropathies over the neonatal and immediate weaning period.

This dissertation follows the style of *Journal of Animal Science*.

Moreover, approximately 50% of the deaths were associated with an intestinal bacterial infection, which was caused primarily by pathogenic stains of *E. coli*. Therefore, compromised immuno-competency at birth, which results in increased susceptibility to infectious pathogens, could have a considerable impact on the survival rate of piglets.

Increasing efficiency and reducing production costs are continually required to enhance profitability of the global pork industry. Hodge (1974) and Boyd et al. (1995) demonstrated that artificially reared neonatal pigs are able to grow at least 50% quicker than those of sow-reared piglets. Additionally, Harrell et al. (1993) has shown that a sow needs to produce 18 kg/d of milk to supply piglets with enough energy to grow at a rate comparable to artificial-reared piglets of the same age. Thus, one of the reasons why piglets are limited in the rate of growth is the unsatisfactory amount of milk produced by the sow. A heavier piglet at birth is more likely to survive, and the heavier piglet at weaning has a greater potential of growing more rapidly at a lower cost and a shorter period between weaning and marketing (Pollmann, 1993). Thus, heavier birth weights were associated with increased probability of preweaning survival (Tyler et al., 1990).

Pluske et al. (1998) suggested that the composition of sow's colostrum and milk limited the potential for lean tissue growth in the piglets. Based on the amino acid pattern in sow's milk, arginine requirement of piglets for growth, and metabolic studies, it is now clear that a deficiency of arginine in the milk is a major factor limiting maximum growth of young pigs (Wu and Knabe, 1994; Wu and Knabe, 1995). Thus, arginine is an essential amino acid for young mammals (Flynn et al. 2002; Southern and Baker, 1983). In addition to arginine, some plant extracts have been reported to have many beneficial effects on increasing the growth rate of postweaning piglets when they are added to their feed (Kong et al., 2010). Nowadays, the *Yucca schidigera* extract, which contains active steroidal saponin components, has been used as a dietary supplement to reduce ammonia levels and increase growth performance of piglets (Cheeke, 2000; Colina et al., 2001).

Many studies have been performed regarding the high survival rate of low-birth-weight pigs, but most of them have not been directed to the efficiency of utilization of dietary nutrients by animals or development of new means to improving their postweaning survival and growth. Therefore, the hypotheses of the current study are that efficiency of nutrient utilization is reduced in low-birth-weight piglets compared with normal-weight-piglets and

that the survival and growth of low-birth-weight piglets can be improved by nutritional modulations.

The objectives of the study are: 1) to evaluate survivability and growth performance of low-birth-weight piglets. 2) To analyze the efficiency of milk utilization (gain/milk) and growth rate of low-birth-weight piglets that could successfully survive during the preweaning period. 3) To determine the effects of natural growth promoter compounds (Yucca schidigera and citrulline) on growth performance of postweaning piglets.

REASONS CAUSING LOW BIRTH WEIGHT IN PIGLETS

A number of factors contribute to low birth weight pigs, including genetic background, parity, nutrition, environment, and management (Foxcroft et al., 2006; Wu et al., 2006). It is generally accepted that uterine capacity and maternal uterine nutrition are two main factors associated with higher occurrence of low birth weight pigs. Johnson et al. (1999), selected pigs for increased ovulation rate and embryonic survival for 11 generations followed by selection for increased litter size for 3 generations; after 14 generations, litter size of the select line had increased by nearly 1.5 live born-pigs and 3 fully formed pigs. Yet, the total litter weight at birth did not show any significant change which indicates pigs in the larger litters are usually smaller. According to the results of his study, litter size can be increased; but, uterine capacity confines the total litter weight.

Increasing litter size and its effects on reduced birth weight in pigs negatively affects the swine industry worldwide. In recent years selection for sow prolificacy, using both genetics and management procedures resulted in increased numbers of live-born pigs by one per litter (10.2 vs. 11.35) from 1998 to 2008 (PIGCHAMP 1998, 2008). In addition to the effect of uterine capacity on birth weight (Johnson et al., 1999), other studies have reported similar associations. A study (n = 60 pigs) which focused on the impact of piglet birth weight on carcass traits, reported pigs from larger litters were heavier at birth vs. pigs born to smaller litters (Bérard et al., 2008). Two large studies (n > 10,000 piglets) reported similar findings; increased litter size was associated with reduced birth weight (Roehe, 1999; Roehe et al., 2009; Quiniou et al., 2002). Holl and Long (2006) concluded that increased litter size

was associated with decreased average birth weight and an increased incidence of pigs weighing less than 0.9 kg at birth.

Based on the combination of increased litter size in U.S. swine production over the last decade and the association between litter size and birth weight, it can be concluded that there are a greater number of low-birth weight pigs within production systems. The impact of these low-birth weight pigs on production are of great economic importance to swine producers.

EFFECTS OF LOW BIRTH WEIGHT ON ECONOMICALLY IMPORTANT PRODUCTION TRAITS

Mortality

The impact of low birth weight on prenatal, preweaning and postnatal mortality has been clearly studied (Wu et al., 2006). Few studies have looked in detail at the impact of birth weight on post weaning mortality. Moreover, some of the studies focused on the relationship between within-litter variation in birth weight and prenatal and pre-weaning survival. Results vary as to which is of greater importance to mortality, individual birth weight or within-litter variation in birth weight. Therefore, the review will focus on both aspects of piglet birth weight and their relationships with mortality.

Milligan et al. (2002) reported increased preweaning mortality is closely related with greater within-litter variation. Effects of increased within-litter variation on increased pre-weaning mortality have been shown to be significant (Roehe and Kalm 2000); however, using individual birth weight in the model analysis of preweaning mortality was much more accurate. Others reported no association between within-litter variation in birth weight and prenatal mortality (Zaleski and Hacker, 1993; Leenhouwers et al., 1999; Le Cozler et al., 2002 Wolf et al., 2008; Arango et al., 2006) or pre-weaning mortality (Pettigrew et al., 1986; Gardner et al., 1989; Knol et al., 2002). No studies have analyzed the potential effects of within-litter variation of birth weight on postweaning mortality.

The effect of within-litter variation on prenatal or preweaning survival is contradicted among different studies. However, most of these studies did not show a significant effect

while others reported small or secondary effects. Therefore, the effect is probably population dependent and is minor to other factors which are more significant to the future prenatal and pre-weaning mortality.

Pre-weaning mortality. Many studies reported a close relationship between reduced piglet birth weight and increased probability of stillbirth in pigs (De Roth and Downie, 1976; Quiniou et al., 2002; Canario et al., 2006). According to Zaleski and Hacker (1993) individual low birth weight does not significantly increase stillbirth but piglets that are born in lower than average litter weight are more susceptible to stillbirth. Asphyxia during parturition is considered as one of the major components of prenatal mortality (Alonso-Spilsbury et al., 2007). Herpin et al. (1996) reported that pigs with higher levels of asphyxia are more susceptible to preweaning mortality than pigs with less asphyxia. De Roth and Downie (1976) showed that pigs with lower birth weight were likely less viable than bigger ones. For that reason, lower birth weight pigs can be more vulnerable to asphyxia during parturition and hence more prone to be stillborn (Leenhouwers et al., 1999; Quiniou et al., 2002).

Increased birth weight has been shown to be directly related with a reduced pre-weaning mortality (Bereskin et al., 1973; Pettigrew et al., 1986; Gardner et al., 1989; Roehe and Kalm, 2000; Quiniou et al., 2002). There are a lot of possible biological explanations for this observation in both prenatal and postnatal life. Vitality and energy consumption are two major postnatal factors. De Roth and Downie (1976) showed lower birth weight pigs had lower viability scores right after birth hence the higher chance of pre-weaning mortality. It has been demonstrated that lower birth weight pigs consume less colostrum which increases the possibility of pre-weaning mortality (Devillers et al., 2005; Devillers et al., 2007). Besides crushing of piglets by the sow which is one of the most common reasons of early life mortality, insufficient colostrum consumption would be among the most important causes (Le Dividich et al., 2005). Although pre-weaning mortality occurs mostly early in lactation reduced milk consumption is also considered a limiting factor with respect to future growth (Roehe and Kalm, 2000).

It has been shown that lighter birth weight pigs get less milk due to competition with heavier ones (Hartsock and Graves, 1976). Milk intake is very important for the survival of

the piglets. Even though creep feed is available prior to weaning the piglets still highly rely on the sow's milk in order to meet their energy and nutrient requirements (Sorensen et al., 1998). Birth weight not only plays a vital role in prenatal and pre-weaning mortality but it also is a prediction of future growth and performance.

Post-weaning mortality. There are only a small number of studies regarding the effect of birth weight on mortality after weaning and during nursery the phase. Larriestra et al. (2006) and de Grau et al. (2005) analyzed potential effects of weaning weight on mortality during the nursery phase. Lighter pigs at weaning were more susceptible for mortality during nursery phase. As discussed, many studies reported close associations between birth weight and weaning weight. For that reason, these associations can explain an impact of birth weight on mortality during the nursery phase. Smith et al. (2007) directly studied the impact of birth weight on nursery mortality. Based on their results pigs in the lightest birth weight category had a lowest survival rate during the nursery phase but the effect of birth weight on mortality was not consistent among all birth weight categories.

Based on the association between birth weight and mortality prior to weaning most of the light birth weight pigs cannot survive till the nursery period or beyond. Therefore, analyzing post weaning data would not be accurate because the majority of light birth weight pigs do not survive post weaning or especially beyond the nursery phase.

Body Weight and Growth

A number of studies have estimated the phenotypic association between birth weight and future BW or growth. Studies have used a variety of populations and comprised of a number of different sample sizes and experimental designs. However, there is an agreement across all studies; increased birth weight is associated with increased BW at a constant age or fewer days to reach a constant BW. Because findings were in agreement among studies, this review will be condensed.

In the majority of these studies, birth weight classifications consisted of heavy vs. light or heavy vs. medium vs. light. Effects of birth weight on subsequent body weight were not identical in magnitude across studies; however, pigs in the heavier birth weight categories

had greater BW measured later in life (Powell and Aberle, 1980; Wolter et al., 2002; Nissen et al., 2004; Poore and Fowden, 2004; Gondret et al., 2005 and 2006; Rehfeldt and Kuhn, 2006; Bérard et al., 2008; Rehfeldt et al., 2008). Two studies, Quiniou et al. (2002) and Smith et al. (2007), divided pigs into a greater number of categories by 200 g increments and one-half standard deviations, respectively. In both studies, pigs in the heavier birth weight categories were heavier later in life. Quiniou et al. (2002) also analyzed the effect of birth weight as a continuous effect and found a quadratic association which was comparable to the relationship in studies by Schinckel et al. (2007 and 2010). Of note, Quiniou et al. (2002) and Schinckel et al. (2007 and 2010) found that as birth weight increased BW measured later in life increased at a relatively decreasing rate. Based on results of these studies analyzing birth weight as a continuous effect and not categorical, the association between birth weight and future BW is not linear. This potential nonlinear association must be considered when estimating the relationship between birth weight and important production parameters.

The basis for the association between birth weight and future BW is probably a combination of both pre and postnatal effects. One prenatal effect is the number of muscle fibers which is determined prenatally. However, the increase in the size of the muscle fibers impacts growth (Dwyer et al., 1993; Rehfeldt et al., 2000; Herfort Pedersen et al., 2001). Lower birth weight is associated with a reduced number of muscle fibers in pigs (Nissen et al., 2004; Gondret et al., 2005, 2006; Rehfeldt and Kuhn, 2006). Consequently, differences in muscle fibers between pigs of varying birth weights accounts for a portion of the variation in future BW.

Based on the associations described above, light birth weights pigs begin life with reduced potential for future maximum growth. In addition, there are also postnatal factors which potentially impact light birth weight pigs with a further disadvantage with respect to future growth. More specifically, colostrum from the sow provides the newborn piglet with vital energy and maternal antibodies vital to piglet development (Le Dividich et al., 2005).

Several studies reported at least a minor relationship between increased birth weight and the selection of anterior teats (McBride, 1963; Fraser, 1975; Hartsock et al., 1977) which have been shown to produce a greater amount of colostrum (Fraser and Lin, 1984). Pigs reportedly gained more BW when nursing anterior teats (Kim et al., 2000). Other studies have measured colostrum intake and reported reduced intake in lower birth weight pigs

(Devillers et al., 2005, 2007). Furthermore, composition of proteins in colostrum or milk differs between anterior and posterior mammary glands (Wu et al., 2010b). These differences in colostrum intake, protein composition, and nursing activity may further exacerbate the difference in future BW due to piglet birth weight. Thus, pigs begin life lighter, have less potential for future BW, and are further negatively impacted by postnatal environmental factors. All of which lead to light birth weight pigs being considerably lighter at harvest or requiring a greater number of days to reach an appropriate harvest BW.

Feed Intake

Differences in feed intake due to birth weight have been explored in fewer studies than BW. Few studies have collected feed intake on a very large number of pigs with recorded birth weights. In the studies which estimated the association between birth weight and average daily feed intake, experimental designs included a fixed BW as the determinant for the conclusion of test periods. Two studies reported that increased birth weight was associated with increased average daily feed intake during a finishing period (Wolter et al., 2002; Bérard et al., 2008); however, both of these studies reported no differences in average daily feed intake during nursery period. Also, Gondret et al., (2006) and Schinckel et al. (2010) reported no association between piglet birth weight and average daily feed intake. These studies had limitations because BW was used as an off-test constraint. Low birth weight pigs grow slower and take more days to reach a suitable market weight. Consequently, these pigs would require more feed for maintenance that their faster growing contemporaries (NRC, 1998).

Gain to Feed Ratios

Once again the literature is limited regarding estimates of the association between birth weight and feed efficiency. It has been reported that heavier birth weight pigs have greater gain to feed ratio during the finishing period (Wolter et al., 2002; Gondret et al., 2006; Bérard et al., 2008). All three of these studies either began or concluded test periods based on the animals reaching a predetermined BW. In each situation, pigs were used for

calculation of gain:feed ratio when a specified BW was reached. Lighter birth weight pigs required 7 to 12 d more to reach final BW. Reduced gain to feed for lighter birth weight pigs may be attributed to more feed consumed for maintenance during the extra days required. Schinckel et al. (2010) used nearly 2000 pigs housed in pens with individual feed intake recorded with FIRE® feeders, reported feed to gain increased as birth weight decreased. Birth weight was analyzed as a continuous variable, this was the only study to analyze the data this way; however, similar to other studies, pigs were removed from pens for test based on a predetermined BW but not age. Other research has shown no impact of birth weight on efficiency; either for various test periods or the whole trial. Wolter et al. (2002) did report an increase in gain:feed ratio from weaning to 14 kg BW for heavier birth weight pigs but no difference from 25 to 54 kg BW, which is in agreement for Bérard et al. (2008) during the postweaning and growing periods. Similarly, Powell and Aberle (1980) reported no difference in feed to gain during any phase of the trial.

One possible explanation for the increased gain to feed in heavier birth weight pigs during the finishing phase is the reduced number of days during the test period. In each instance of poorer gain to feed during the finishing phase, lighter birth weight pigs were on test for more days. Based on the fact that each day pigs have a basal maintenance requirement of energy (NRC, 1998), light birth weight pigs need more energy to sustain life than normal-birth-weight piglets.

Composition

Exact total body composition is difficult and expensive to determine; however, measures of backfat and muscling are used as predictors. More specifically, real-time ultrasound or actual carcass values of backfat depth and longissimus muscle area or depth are typically collected to predict percent lean. The following summary will focus on associations among birth weight, backfat depth, muscling, and percent lean.

Backfat depth. Published results on associations between birth weight and backfat were highly variable. A study in which pigs were fed ad libitum and harvested at a constant age, reported no difference in BF among pigs differing in birth weight (Rehfeldt et al., 2008). No

difference in fat thickness due to birth weight was also reported for pigs harvested at a constant weight with restricted feeding (Gondret et al., 2005). Powell and Aberle (1980) reported no difference in fat thickness due to birth weight for pigs fed ad libitum to a constant age, but adjusted backfat to a common hot carcass weight. A study utilizing ad libitum feeding and measuring backfat at constant BW reported increased backfat in low birth weight pigs (Gondret et al., 2006). Poore and Fowden (2004) measured backfat at 12 months of age and reported increased backfat in low birth weight pigs; of note this particular study collected backfat measures much later in life than other studies, 12 months of age. Schinckel et al. (2010) used a nonlinear model and reported increased backfat depth in lighter birth weight pigs; once again these pigs were fed ad libitum using FIRE® feeders to a constant BW. The association between birth weight and backfat is affected by the type of feeding and endpoint (age or weight) used to determine when backfat is measured. Pigs measured, either by real-time ultrasound or at harvest, at a constant age did not differ in backfat due to birth weight. However, when a constant weight was used as the constraint, low birth weight pigs, which are older at similar BW, have greater backfat depth.

Muscling. Muscling in pigs is typically reported as either longissimus muscle area or depth. Studies estimating the effect of birth weight on muscling utilized either method but similar results were reported within similar experimental designs. Nissen et al. (2004) and Rehfeldt et al. (2008), again both harvesting at a constant age, reported heavier birth weight pigs had increased muscle mass and longissimus muscle area, respectively. Bérard et al. (2008) and Powell and Aberle (1980) found no difference in muscling between birth weight classes, when measuring at a constant BW or adjusting for HCW, respectively.

Measuring at a constant body weight Schinckel et al. (2010) reporte longissimus muscle depth was greater in heavier birth weight pigs. This is in agreement with studies that did not adjust for or measure at a constant. Reasons for differences among studies with similar designs are unknown. Heavier birth weight pigs with increased muscle mass when not adjusting for BW is likely explained by the association between piglet birth weight and future BW. It is commonly known that heavier BW pigs have increased muscling. Similarly, heavier birth weight pigs have increased BW later in life. When this is not adjusted for, the

association between birth weight and BW results in increased muscling in pigs with heavier birth weights.

Percent lean. As previously discussed, backfat and muscling are absolute measures used to predict composition or more specifically percent lean. Therefore, it is important to discuss the impact of birth weight on measures of percent lean. Again, results were not consistent across studies. However, most studies reported no difference in percent muscle or percent lean due to differences in birth weight (Powell and Aberle, 1980; Nissen et al., 2004; Gondret et al., 2005; Bérard et al., 2008; Rehfeldt et al., 2008). Rehfeldt et al. (2008) did report a tendency for a birth weight x sex interaction ($P = 0.07$) for lean meat percent where barrows did not differ across birth weight but gilts in the heaviest birth weight category had a greater percentage lean meat than gilts in either the middle or low birth weight categories. In line with those findings, Gondret et al. (2006) also noted reduced lean meat content for low vs. heavy birth weight pigs. In these two studies, differences were observed only for gilts not barrows. Most recently, Schinckel et al. (2010) estimated a significant nonlinear effect of birth weight on estimated percent lean. The authors reported associations between birth weight and estimated percent lean differed between sexes. Based on graphical depictions, it appears the effect of birth weight on estimated percent lean was greater in gilts compared to barrows.

GASTROINTESTINAL DEVELOPMENT IN PIGLETS

The piglet gastrointestinal tract, especially the small intestine, undergoes accelerated growth and functional maturation in the immediate post-natal period. Of note, due to stressful factors, intestinal atrophy and damage occur within one week after weaning (Xu et al. 2000). At birth, piglets must adapt to the initial transition from primarily parenteral to solely enteral nutrition (Zhang et al., 1997). After weaning, the neonates abruptly experienced another transition from a liquid, highly digestible diet (milk) to a solid diet (often plant-based) (Xu et al. 2000). It is therefore vital for piglet survival that the gut matures and adapts to changes in both diets and environment.

GASTROINTESTINAL DEVELOPMENT IN THE PRE -WEANING PIG

In the neonatal pig during the immediate postnatal period, there is a large increase in all tissue weights. For example, Zhang et al. (1997) found that most initial growth occurs within the first six hours of suckling. A study by Xu et al. (1992) revealed that stomach tissue weight of three day-old piglets increased up to 54% with a 23% increase in body weight in comparison with newborn pigs. Rapid postnatal growth of the intestines has been attributed to endocytosis of ingested immunoglobulins, protein synthesis and mucosal hyperplasia (Burrin et al. 1992). Colostral proteins are retained in protein dense intracellular granules in enterocytes lining the gastrointestinal tract (Zhang et al., 1997). This is supported by observed increases in protein concentration coupled with a decrease in DNA and RNA in small intestine mucosa of colostrum fed piglets in comparison with unsuckled pigs (Wang et al., 1996). Decrease in the specific absorptive capacity per unit of mucosal tissue mass in newborn piglets is due to a dilution effect of retained colostral proteins rather than a loss of brush boarder transporters (Xu et al., 1992).

Porcine colostrum and milk contain highly digestible nutrients and bioactive compounds such as immunoglobulins and lysozymes which protect the gastrointestinal tract from pathogenic microorganisms (Mubiru et al., 1997 and Xu et al., 2000). Compared to non-suckled piglets, those fed colostrum exhibited active cell proliferation, indicated by a 39% increase in mucosal DNA (Wang et al., 1996). It was suggested that this rapid proliferation seen in the small intestine may partly be attributed to trophic factors found in colostrum (Wang et al. 1996), such as epidermal growth factor (EGF), insulin- like growth factor-I (IGF-I), IGF-II and insulin. Orally administered growth factors stimulate gastrointestinal tract maturation (Odle et al., 1996 and Xu, 2000). For example, enhanced digestive enzyme activity, improved gastric secretory capacity (Xu et al., 1992 and Wang et al., 1996) and increased tissue weights have been demonstrated in several studies.

Neonatal pigs have an immature immune system and yet are constantly challenged by potential pathogens in the environment. It is therefore vital that immunity is acquired by piglets through intake of colostral immunoglobulins. The immunological profile of colostrum, e.g. IgG concentration, and the ability of the piglet to consume enough colostrum

before gut closure, which occurs within 2 to 3 days of postnatal life (Westrom et al., 1984; Xu et al., 2000) is of primary importance in determining piglet survival.

PRE-WEANING ENZYME ACTIVITY

In terms of maturation of intestinal digestive enzymes, age is a significant factor affecting mucosal hydrolytic enzymes (Wang et al., 1996). In 3-day-old colostrum-fed piglets, Wang et al. (1996) observed a significant increase in lactase and alkaline phosphatase activities and this result was not observed for piglets fed trypsinized colostrum, indicating that stimulation of these enzymes may be due to colostrum ingestion and that colostrum contains trypsin- labile substances such as insulin and IGF's. However, it was also observed that maltase activity within 3 days of postnatal life increased significantly with age irrespective of diet (Wang et al., 1996). Sucrase was undetectable throughout the intestine at three days of age. Colostrum-borne insulin may have an ability to stimulate gastrointestinal enzyme maturation in suckled piglets (Shulman, 1992).

POST-WEANING PIGLET

A second stressful period for the piglet is weaning. Piglets are placed in a new environment away from their mother, mixed with piglets from other litters, and presented with different sources of food and water. They will also come into contact with pathogens to which they may have no resistance, resulting in post-weaning disease, which usually presents itself as scours. Disease is usually more prevalent during this period as weaning also coincides with a natural drop in passive immunity from the sow before piglet immunity is fully developed. The piglet is therefore more susceptible to the pathogenic organisms it encounters in its new environment. This combination of factors results in reduced feed intake in the immediate post-weaning period, which to the farmer is a concern as piglet growth does not reach its potential. This lack of nutrition and poor general immunity may ultimately result in death if the piglet is not able to adapt to this new situation.

SMALL INTESTINE MORPHOLOGY

It has been well documented that at weaning there is a marked reduction in villus height and increased crypt depth in the small intestines. Villus morphology has been observed to change from long finger-like projections before weaning to shorter leaf or tongue-like structures post-weaning (Hampson, 1986 and Xu et al., 2000). The extent of observed structural changes appears to vary along the length of the small intestine. The changes in villus height are more prominent in the proximal and medial region, 2%, 25% and 50% along the small intestine (Hampson, 1986). In contrast, the increase in crypt depth is more prominent in the distal region (Pluske et al., 1997). The ratio of villus height to crypt depth is greatly reduced in weaned piglets compared to unweaned controls (Hampson, 1986). These morphological changes appear to be affected by age at weaning with more conspicuous changes being noted in younger piglets. Namely, early weaned pigs are subject to a greater degree of intestinal atrophy during this period. The younger the piglet, the less developed the gut will be, and the harder it is for the piglet to physically adapt to cope with the increase in gut capacity and digestive capability required for digestion of the weaner diet. Increased crypt depth is believed to be a result of increased rate of cell loss at the villi apex, leading to crypt cell hyperplasia and therefore increased crypt depth (Hampson, 1986; Pluske et al., 1997). The reduction in villus height and subsequent more rapid turnover of cells result in a reduction in the absorptive capacity of the intestine, as cells at the villus apex have not matured to reach their full absorptive and digestive capacity. This statement is supported by the work of Smith (1984) who observed that postweaning villus enterocytes had a reduced ability to absorb alanine.

It has been suggested that the morphological changes occurring after weaning are partially a result of an inflammatory response due to hypersensitivity to certain dietary antigens (Kenworthy et al., 1976). However these changes have been documented in the absence of an inflammatory response (Hampson, 1986). Kelly et al. (1991) concluded that gut function, anatomy and morphology alter in response to the level of feed intake, with decreased feed intake and a cortisol surge causing the changes seen in the weaned piglet gut.

POST-WEANING ENZYME ACTIVITY

Regarding post-weaning mucosal enzyme activity, reductions in the specific activities of lactase and sucrase have been shown immediately post-weaning coupled with an increase in the activity of maltase thought to be due to substrate induction (Xu et al., 2000). Along with the ability to secrete digestive enzymes, there must also be adaptation to increase the physical capacity of the gastrointestinal tract. This will help the piglet to have a successful transition from milk-based to a grain-based diet (Cranwell, 1976, 1995). The diet-induced change in digestive enzyme profile results from changes in actual dietary components (Ferraris, 2001).

FUNCTIONS OF AMINO ACIDS

Amino acids are molecules that contain both amino and acid groups. Amino acids are the primary structural building units of proteins. They form short polymer chains, peptides or polypeptides, which subsequently form proteins. There are generally 20 different amino acids in protein structures. New findings about biochemical and molecular actions of amino acids have provided useful knowledge for designing new means to improve health and growth. Arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine are nutritionally indispensable or essential amino acids for piglets. The pig body cannot synthesize all of these amino acids except arginine so they must be provided from the diet. Conversely, the amino acids that can be synthesized in the body are termed nutritionally dispensable or nonessential, including alanine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, and tyrosine. Essential amino acids have been highlighted for swine nutrition.

The main function of dietary amino acids is to stimulate muscle protein synthesis. Individual amino acids have been proposed to work as signaling molecules that regulate mRNA translation. For example, leucine has been suggested to have a signaling role in the simulation of muscle protein synthesis by enhancing availability of specific eukaryotic initiation factors (Anthony et al., 2000). Some amino acids have been implicated in immune

function (Li et al., 2007) and some are important precursors of neurotransmitters and certain hormones (D'Mello, 2003; Wu, 2009).

Sow's colostrum and milk contain large amounts of glutamate and glutamine, but a negligible amount of ornithine and citrulline (Wu and Knabe, 1994). Glutamate serves as the main medium in amino-N exchange and is readily converted into other nonessential amino acids. It plays an important role in protein metabolism (Heger, 2003). Dietary glutamate is catabolized almost completely in enterocytes of piglets to yield ATP, CO2, proline ornithine, citrulline, and arginine (Wu, 1998). Concentrations of proline and alanine are relatively high in piglet's plasma compared with glutamate. Glutamate and acetyl-CoA are substrates for synthesis of N-acetylglutamate (NAG) within liver and enterocytes, therefore up-regulating ammonia detoxification and arginine synthesis, respectively (Meijer et al., 1990; Wu and Morris, 1998).

Glutamine was utilized by the enterocytes of the small intestine as major energy supply (Wu et al., 1994). Glutamine could contribute more energy as ATP to enterocyte and gastrointestinal development than glucose (Wu et al., 1995). Wu et al. (1995) reported that glutamine is a major substrate for synthesis of citrulline and arginine in enterocytes of piglets from the day of birth to seven days old, and suggested the endogenous synthesis of arginine is important for the animal's optimal growth particularly during the neonatal period when requirements for arginine are high. Additionally, glutamine has a role as an immune modulator (Li et al., 2007). Glutamine is also required for the functioning of monocytes and macrophages, lymphocytes, and neutrophils (Alverdy, 1990). High concentrations of glutamine in the plasma could help piglets sustain the normal function of lymphoid organs and lymphocytes.

Arginine is generally considered nutritionally essential for neonates, because its synthesis is inadequate for metabolic needs (Wu et al., 2004). Arginine is the most abundant nitrogen carrier in tissue protein and is a major factor regulating maximal growth of young mammals (Flynn et al., 2002 and Wu et al., 1999). Formation of nitric oxide from arginine has been shown to regulate inflammation, and exogenous sources of arginine may help increase monocyte and lymphocyte proliferation and T helper cell formation (Suchner et al., 2002).

Proline is not considered a nutritionally essential amino acid (and Chung and Baker, 1993; NRC 1998). Previous study indicated there was no difference in piglet growth performance between proline-free diet and proline supplementation diet (Murphy, 1992). This is likely due to inadequate provision of several limiting amino acids in the diet. However, young pigs that weighed 1 to 5 kg were unable to synthesize proline to meet their requirements (Ball et al., 1986); thus, dietary proline was required for young pigs. In support of view, supplementing 1% proline to the diet for postweaning pigs enhanced intestinal and whole-body growth (Wu et al., 2010c).

Cysteine, tyrosine, and glutamine are nonessential amino acids (NRC, 1998), but their functions should be considered as important as essential amino acids. Cysteine can reduce the need for its precursor, methionine. Moreover, reports have indicated that methionine's metabolite, cysteine, can satisfy approximately 50 % of the need for total sulfur amino acids (Chung and Baker, 1992). Macrophages may release cysteine under catabolic conditions, and cysteine may enhance intracellular concentrations of glutathione in lymphocytes (D'Mello, 2003).

DIGESTION OF AMINO ACIDS IN PIGLETS

The digestion of protein starts in the gastric lumen, continues in the small intestinal lumen, and is completed at the brush-border membrane of the enterocytes. Hydrochloric acid and gastric proteases initiate protein hydrolysis in the gastric lumen. Hydrochloric acid is secreted by the gastric parietal cells. Hydrochloric acid activates gastric proteases and denatures the dietary protein. The gastric secretory capacity increased more rapidly after pigs were fed with creep diet rather than fed by sow (Carnwell, 1976). The low gastric secretory capacity at birth may relate to immaturity of the parietal cells in newborn pigs. The acidity of gastric contents in the post absorptive state is about pH 3 to 5 in piglets during early postnatal period due to low gastric secretory capacity and the high buffering capacity of sow's milk.

Gastric proteases are secreted by the chief cells in the gastric gland. Pepsin A, pepsin B, pepsin C, and chymosin are four critical proteases for protein digestion. Chymosin has strong milk-clotting ability but weak proteolytic activity. Clotting milk by chymosin occurs through a specific cleavage of κ-casein. Milk-clotting may regulate gastric emptying and

stimulate gastric development through gastric distention (Stadaas and Schrumpf, 1974). Prochymosin has the highest concentration at the time of birth. The concentration of prochymosin in fetal pig gastric tissue is detected as early as at 80 d of gestation (Sangild et al., 1994).

Pepsinogen A replaces the prochymosin to become the dominant protease in the gastric tissue of pigs by the 5th wk of age. The proteolytic activity of neonatal piglets is relatively low in the stomach due to gastric acid secretory capacity and the small amount of pepsinogen A secreted. The bioactive compounds, such as immunoglobulin, hormone, growth factors, and bioactive peptides presented in the colostrum and milk are able to pass undegraded because of the low proteolytic activity.

Therefore, postnatal gastrointestinal development in neonatal pigs possibly could be regulated by those bioactive compounds (Xu et al., 2000).

The pancreas also secretes many types of proteases, including trypsin, chymotrypsin, elastase and carboxypeptidase A and B. Pancreatic proteases are secreted as proenzymes and are activated in the lumen of the small intestine. The starter phase of protein digestion in the small intestine begins when activated pancreatic proteases in the small intestine cleave peptide bonds on the carboxyl side of amino acids. The carboxypeptidases remove a single amino acid from the carboxyl-terminal end of proteins and peptides. Oligopeptides generated by gastric and pancreatic proteases are further digested by the membrane peptidases to free amino acids or di- and tri-peptides before being absorbed. Aminopeptidase N is the most abundant membrane peptidase that cleaves amino acids from the N-terminus of oligopeptides.

ABSORPTION OF AMINO ACIDS IN PIGLETS

Absorption of amino acids by pigs mainly occurs in the proximal region of the small intestine (Buraczewska, 1981). Intestinal mucosal cells absorb amino acids via active transport, simple diffusion, and facilitated diffusion. There are at least four sodium-dependent amino acid transporters in the luminal plasma membrane of the intestinal mucosal cells responsible for transporting amino acids into the cytoplasm (Herdt, 1992). Amino acids are subsequently oxidized or pass to the portal circulation for body use. After amino acids

have been absorbed, they are used mainly for tissue protein synthesis, synthesis of enzymes, hormones, and other metabolites, and deamination or transamination and use of the carbon skeleton for energy.

A major function of the enterocyte lining the villi in the proximal region of the small intestine is to absorb antibodies from the sow's colostrum (Baintner, 1986). Immunoglobulins are macromolecules that are absorbed preferentially by the small intestine. The capacity for macromolecular absorption is very important in newborn pigs, which rely on passive immunity from colostral immunoglobulins. The fetal type of enterocytes responsible for macromolecular uptake is present at birth. Nineteen days after birth, the fetal type of enterocytes change to the adult type of enterocytes, which have the capacity to digest and absorb nutrients (Smith and Peacock, 1980). From 24 to 36 h after birth, the transfer of macromolecules from the intestinal epithelium into the blood is decreased dramatically (Ekström and Weström, 1991). Gut closure is associated with the postnatal replacement of fetal intestinal enterocyte with cells that are incapable of internalizing macromolecules. Newborn pigs have a longer turnover time of enterocytes because the small intestine of older pigs is larger with longer villi, and damaged villi in the small intestine would be replaced with new villi at a faster rate than fetal-type villi.

Amino acids also may be able to be absorbed to some extent in the large intestine. The proximal colon and the cecum in the newborn piglet have villus-like structures that are lined with columnar epithelium, and the epithelium exhibits well-defined mircrovilli on the luminar border. As the newborn piglets grow older, the villus structures are no longer present, and the mucosal surface has a relatively flat appearance (Xu et al., 1992). The morphological changes coincide with the transient ability of the large intestine of newborn pigs to absorb amino acids because the proximal colon has many of the properties of a small intestine at birth (James and Smith, 1976). Colonic transport of amino acids seems to represent a transient overspill function of the small intestine. Darragh et al. (1994) reported that the capacity of the proximal colon to absorb amino acids is reduced to an insignificant level by the age of 15 d.

BIOAVAILABILITY OF AMINO ACIDS IN PIGLETS

The protein and amino acid are not fully digested and absorbed. Undigested amino acids from the small intestine would be used for metabolism by microbes for the animal's growth and development. Absorbed amino acids also are not fully metabolically available to extraintestinal tissues. Therefore, only a portion of the amino acids in the diet is biologically available to the pigs (NRC, 1998). To formulate a highly-effective pig diet, the bioavailability of amino acid content must be known. The availability of amino acids is determined by digestibility measured at the end of the small intestine or from the pig's fecal excretion (Low, 1982). Apparent ideal digestibility is measured at the end of small intestine and excludes the endogenous or exogenous origin of the indigestible nitrogen or amino acid. As a consequence, a low-protein diet is undervalued relative to a high-protein diet; however, apparent ileal amino acid digestibility is a more sensitive approach than fecal digestibility (Mosenthin and Rademacher, 2003). On the other hand, true digestibility coefficients are higher than apparent digestibility. True or standardized digestibility subtracted basal endogenous or exogenous losses from what is collected at the end of small intestine (Rademacher et al., 1999) The amount of amino acid, especially essential ones, in the diet and the relative proportions between them determine the deposition of protein in pigs.

Amino acids from the diet are utilized by the gastrointestinal tract for maintenance and tissue accretion. Knowing gross amino acid composition in the diet cannot provide a clear indication of the amount of amino acids nutritionally available to the pigs. Determining digestibility for each amino acid in the diet is used to correct the gross amino acid composition. Thus, amino acids absorbed by pigs and amino acid requirements can be determined. Further, new methods and technologies can be developed for enhancing pig growth rate.

METABOLISM OF AMINO ACIDS IN THE SMALL INTESTINE

Terminal digestion and absorption of dietary nutrients including protein and amino acids is accomplished primarily in the small intestine. Stoll et al. (1998) demonstrated that catabolism dominates the first-pass intestinal utilization of dietary essential amino acids.

Baracos (2004) depicted the important implication of intestinal metabolism having the ability to distribute large amounts of amino acids during enternal and parenteral feeding. The intestinal capacity for amino acid metabolism has great adaptation for amino acid mixture in the first pass under conditions of enteral feeding.

Under parenteral feeding, the total amino acid requirement of the whole body is reduced and first-pass metabolism is no longer contributing to balancing the incoming amino acid mixture because of the dramatic atrophy of the intestine (Baracos, 2004). Wu (1998) concluded several points relative to the intestinal mucosal amino acid catabolism. First, the small intestinal mucosa plays an important role in degrading arginine, proline, branched-chain amino acids, and other essential amino acids. Glutamate, glutamine, and aspartate in the diet are catabolized by the small intestine mucosa. In addition, dietary amino acids are the major fuel, rather than glucose, for the small intestine and are the essential precursors for intestinal synthesis of nitric oxide, polyamines, purine, and pyrimidine nucleotides (Burrin and Reed, 1997). Furthermore, intestinal amino catabolism plays an important role in modulating availability of dietary amino acids to extraintestinal tissues (Wu, 1998).

UREA CYCLE AND ARGININE METABOLISM

The urea cycle, also known as the ornithine cycle, is a cycle of biochemical reactions occurring in the liver of fetal and postnatal pigs, as well as the small intestine of postweaning pigs. This cycle functions to produce urea from ammonia (NH_3 plus NH_4^+). Organisms that cannot directly excrete large amounts of ammonia into the surrounding environment usually have to convert ammonia to some other substances, like urea or uric acid, depending on species. The cycle comprises a series of reactions involving the formation of arginine, ornithine, citrulline, and argininosuccinate.

Arginine can be synthesized endogenously from glutamate via the intermediates, which are pyrroline-5-carboxylate, ornithine, citrulline, and argininosuccinate. Pyrroline- 5-carboxylate synthase and N-acytylglutamate synthase are the two key regulatory enzymes in the intestinal synthesis of citrulline (Wu et al., 1994). The gut is almost the exclusive site for synthesis of citrulline from glutamine/glutamate and proline in pigs.

Nitric oxide is synthesized from arginine. Nitric oxide may play an important role in the responses to particular antinutrional factors. Moreover, it also plays a key role in cardiac function, neurotransmission, vasorelaxation, immunocompetence, male reproductive performance and gut motility.

Plasma urea is recycled throughout the gastrointestinal tract in the pig (Deutz et al., 1998). The liver is thought to be the primary site for endogenous urea production. The upper villus enterocytes were found to have the capability of synthesizing urea in postweaning pigs (Davis and Wu, 1998). Urea synthesized by the enterocytes is excreted into the gastrointestinal lumen and may be utilized by intestinal microorganisms and converted to microbial protein. Microbial protein can be used by the pig for body protein accretion (Metges, 2000). Ammonia is produced through microbial deamination of amino acids and urea. Plasma ammonia was found to be relatively low in neonatal pigs compared with weaning pigs (Wu, 1995). The gastrointestinal urea recycling and intestinal microbial production of ammonia are relatively low in neonatal pigs, resulting in a relatively high plasma urea concentration.

AMINO ACID REQUIREMENTS FOR NURSERY PIGLETS

Protein deposition in the piglet body primarily uses protein from the diet. Relatively large intakes of protein and energy are required by neonatal piglets for sustaining their rapid growth rate. The energy density of the diet could influence the voluntary feed intake of neonatal pigs. To satisfy the requirement for energy, feed intake increases when the dietary energy is low. The gut capacity of neonatal pigs would also limit the feed intake. Piglets may not be able to consume sufficient amounts of a diet with a low energy density to maintain their optimal growth rate. Essential amino acids cannot be synthesized endogenously by neonatal pig and needed to be provided in the diet. Therefore, an adequate supply of essential acids must be ensured while considering dietary protein requirements.

Growth models cannot be used to estimate energy or amino acid requirements for neonatal pigs because there is not sufficient information on biological relationships for neonatal pig less than 20 kg of BW. However, total dietary lysine required between 3 and 20 kg of BW can be estimated by the equation given by the NRC (1998). The estimation yields

1.45% lysine at 5 kg, 1.25% lysine at 10 kg, 1.15% lysine at 15 kg, and 1.05% lysine at 20 kg of BW.

AMINO ACID NEEDS FOR GROWTH OF PIGLETS

Sow's milk is thought to provide adequate amino acids and basic nutrients needed for the growth of neonatal pigs. However, Hodge (1974) and Boyd et al. (1995) demonstrated that the artificially reared neonatal pigs are capable of growth rates at least 50% greater than those of sow-reared piglets. From eight days old, piglets had exhibited sub-maximal growth, which may have resulted from inadequate intake of protein or energy from the sow's milk (Boyd et al., 1995). Furthermore, arginine is an essential amino acid for the maximal growth of young mammals, but the ratio of arginine to lysine on a gram basis was 0.35 ± 0.02 and 0.97 ± 0.05 in sow's milk and seven days old piglets, respectively (Wu et al., 1999). Available evidence shows that there are low levels of arginine in sow's milk and neonatal pigs must synthesize substantial amount of arginine for their growth.

ENDOGENOUS SYNTHESIS OF ARGININE

Arginine is an essential precursor for the synthesis of proteins and other significantly important molecules such as nitric oxide, urea, ornithine, proline, polyamines, glutamate, creatine, agmatine, and dimethylarginines). Arginine or its effective precursor citrulline plays an important role as nutritionally essential compounds for growth and health of animals.

Even though arginine is formed in the liver via urea cycle, but there is no net synthesis of arginine in the liver due to high activity of enzyme arginase which rapidly hydrolyses arginine into ornithine and urea. Instead the net synthesis of arginine occurs in epithelial cells of small intestine where the activity of arginase is absent. In neonates most of citrulline synthesized in enterocytes (mucosal epithelial cells of small intestine) is converted locally to arginine due to high activities of argininosuccinate lyase (ASL) and argininosuccinate synthase (ASS) and absence of arginase activity. The intestinally derived citrulline and arginine are both similarly effective as a source of arginine for extrahepatic

tissues due to low uptake of physiological concentrations of arginine by the liver (Wu and Morris 1998).

ARGININE AND PROTEIN SYNTHESIS

Arginine is considered an essential amino acid for young pigs (Wu et al., 2004) but is severely deficient in milk-fed piglets (Flynn et al., 2000) due to relative low concentrations in milk protein and reduced intestinal release of citrulline (an effective precursor of arginine) (Wu and Knabe, 1995). Recent studies have demonstrated that enhanced protein accretion in skeletal muscle and the whole body of milk-fed piglets can be achieved by elevating plasma levels of arginine through either dietary arginine supplementation (Kim and Wu, 2004; Wu et al., 2007) or enhancing endogenous arginine synthesis (Frank et al., 2007). Furthermore, arginine can increase protein synthesis in the small intestine of neonatal pigs (Rhoads et al., 2007) partly through activating mTOR and other kinase-mediated signaling pathways (Ban et al., 2004; Tan et al., 2010). Likewise, dietary supplementation with L-arginine can enhance the mTOR signaling pathways in skeletal muscle of neonatal pigs (Yao et al., 2008). Thus, arginine is a major factor that limits maximum growth of young mammals.

It remains unclear how arginine stimulate the mTOR signaling in cells. However, available evidence shows that dietary arginine supplementation affected the phosphorylation of 4E-BP1 protein in piglet muscle (Yao et al., 2008). When 4E-BP1 is phosphorylated, it is dissociated from the inactive eIF4E.4E-BP1 complex, thus releasing eIF4E for binding with eIF4G to form the active eIF4G.eIF4E complex (Gingras et al., 1999; Raught et al., 2001; Raught et al., 1999). Therefore, in response to arginine supplementation, intramuscular concentrations of the inactive eIF4E.4EF-BP1 complex were reduced while the formation of the active eIF4G.eIF4E complex was enhanced in milk-fed neonatal pigs increased (Yao et al., 2008). Ultimately, arginine stimulates the formation of the 43S complex to initiate protein synthesis in skeletal muscle (Cochard et al., 1998).

Arginine effectively stimulates secretion of insulin and somatotropin (Cochard et al., 1998). It has been demonstrated that both insulin (Garlick et al., 1983; Harmon et al., 1984; Karinch et al., 1993) and amino acids (Davis et al., 1998; Wray-Cachen et al., 1998; Davis et al., 2002) can regulate protein synthesis in piglets. However, Yao et al (2008) did not

observe any changes in circulating levels of insulin and amino acids other than arginine in arginine-supplemented piglets. Additionally, an increase in plasma arginine concentrations positively enhanced the growth of neonatal pigs in the absence of a change in plasma levels of insulin or growth hormone (Kim and Wu, 2004; Frank et al., 2007). Therefore, arginine alone has its potent effect on stimulating muscle protein synthesis. In support of this notion, emerging evidence from studies with cultured muscle cells shows that arginine can directly stimulate the phosphorylation of proteins through the mTOR signaling pathway (Jobgen, 2007; Tan et al., 2010). However, it is possible that the maximum effect of dietary arginine supplementation on muscle protein synthesis and growth may be partially mediated by elevated levels of the circulating anabolic hormones via the insulin signaling pathway. This possibility can be examined by using the in vivo techniques of insulin and amino acid clamps developed by Davis et al. (2010) for studies with neonatal pigs (Yao et al., 2008).

YUCCA SCHIDIGERA AS AN AGENT TO IMPROVE DIGESTION

It has been shown that plant extracts have many health beneficial effects both in humans and animals (Platel et al., 1996). Plant additives have been largely used as feed additives to improve palatability. It implicates that sows could have a higher feed intake and therefore more production of higher quality milk. This possibly will have a further positive effect on subsequent piglet growth rate and immunity as well as reducing the occurrence of postweaning scours. *Yucca schidigera* is a native plant of the Baja California desert in Mexico and the Mojave Desert in California, Arizona and Nevada, in the United States. Steroidal saponins and glycocomponents are its two major components. Steroidal saponins have highly tensoactive properties that play essential roles in animal nutrition. As a result of their strong surfactant power; the cell membranes of the intestinal wall become able for more effective absorption of nutrients (Johnston et al., 1981; Oleszek et al., 1994), which also enhances the intestinal flora activity, improving the digestive process. Glycocomponents are molecular structures highly thermostable which are highly capable to capture ammonia molecules in the digestive tract and in the metabolic processes, neutralizing its noxious effects and converting it into another type of non-toxic nitrogenated compounds, hence improving the intestinal conditions. Therefore, the flora increases its degrading activity that

results in a further digestion. At the same time, these compounds reduce the amount of ammonia released to the environment by around 34%, as well as hydrogen sulfide (50%) and other toxic gasses produced in the degradation process of the excretions, improving the environmental conditions of the confinement areas and bringing, therefore, better production conditions and better productive parameters. A study was carried out by ITPSA with 4500 male pigs during 90 days, in Jalisco, in Central Mexico. Adding 100 to 120 g/t of feed of CAPSOGENIN BIOPOWDER, a Yucca extract based product, showed a significant reduction for the levels of environmental and metabolic ammonia, diminishing the appearance of respiratory illnesses and improving nutrient absorption, feed conversion and daily weight gain. Other studies carried out by ITPSA and also by other authors (Hale et al., 1961; Dziuk et al., 1981; Johnston et al., 1981; Goodall et al., 1982; Al-Bar et al., 1993) have also shown improvements in growth and feed efficiency when adding between 31 and 155 ppm extracts of *Yucca schidigera* in diets for broilers, turkeys, rabbits, lambs or cattle. In layer hens also an increase in egg production was observed (Rowland et al., 1976). Decreased levels of ammonia release to the environment as well as improved fecal aroma have also been reported in horses (Glade, 1992), dogs and cats (Lowe et al., 1997).

Yucca is currently used as a dietary supplement for livestock and companion animals, primarily for ammonia and odor control. However, at present, a positive effect of Yucca supplementation on pig growth has not been demonstrated. Yucca saponin has also strong antiprotozoal activity and may serve as a successful defaunating agent for ruminants (Wallace et al., 1994). The mechanism of action has been proposed to involve the forming of irreversible complexes with cholesterol in the cell membranes of all microorganisms except bacteria, causing its breakdown and cell lysis (Cheeke, 1999). The antiprotozoal activity requires the intact saponin structure. However, it can be hydrolyzed by rumen bacteria, removing the carbohydrate side-chains, and rendering them inactive against protozoa. This may result from adaptation of bacterial metabolism to utilize saponins in the diet (Hristov et al., 1999). Therefore, one strategy for retaining antiprotozoal activity could be to feed saponins occasionally, to suppress protozoa but without continuous presence of saponins to induce bacterial adaptation (Cheeke, 1999). As a result of suppression of those rumen protozoa, dietary saponins increase the outflow of bacterial protein from the rumen to the

intestine, therefore more amount of amino acids will be available for absorption (Wallace et al., 1994).

Yucca Schidigera extract has been used in animal production as a factor encouraging friendly bacteria growth and reducing ammonia production in the gastrointestinal tract and fecal odors in animal excreta (Cheeke, 2000, Colina et al., 2001). These effects are mainly due to carbohydrate components and stilbenes that have urease-inhibiting properties (Oleszek et al., 1999, Cheeke, 2000). Yucca extract influences nitrogen metabolism through the reduction of urea and ammonia in serum of cows (Hussain and Cheeke, 1995) rabbits (Hussain et al., 1996) and in rats (Killeen et al., 1998). In pigs, increased growth rate and improved feed conversion efficiency (Cole and Tuck, 1995) as well as inhibition of Gram-positive bacteria and reductions in numbers of pigs born dead have been reported (Cline et al., 1996). A previous trial by Ilsley et al. (2002) showed that the spices capsaicin, oregano and cinnamic aldehyde (cinnamon) present in the Xtract additive were effective in improving pre-weaning piglet performance when fed in the lactating sow diet in comparison to feeding other or no additives. Capsaicin has been shown to have a stimulatory effect on the digestive system inducing small intestine contraction via neural activation (Bartho et al., 1999). It seems feasible to suggest that extracts such as yucca or their metabolites will be more likely to appear in sow's milk after monogastric digestion in comparison to ruminants where the supplement is first subjected to microbial digestion.

In ruminants, Yucca extract can also stimulate growth of certain bacteria, as *Prevotella ruminicola, Selenomonas ruminantium* (Wallace et al., 1994) and Bifido bacteria (Grandhi et al., 1998), and suppress others, as *Streptococcus bovis* and *Butyrivibrio fibrisolvens* (Wallace et al., 1994). The antibacterial properties are most pronounced against gram-positive bacteria, with an action similar to the ionophores. Nevertheless, the mode of action of antibacterial effects of saponins seems to involve membranolytic properties, rather than simply altering the surface tension of the extracellular medium, therefore being influenced by microbial population density (Killeen et al., 1998).

As digestibility of dietary fiber is not adversely affected in ruminants when supplementing the diet with Yucca extract, reducing protozoal populations in cattle improves nitrogen utilization in the rumen and increases microbial protein flow to the intestine (Hristov et al., 1999), thereby enhancing overall growth performance, and acting as a growth

promoter (Goodall et al., 1982). Therefore, in agreement with the previous reports, yucca exerts its ammonia reduction and growth stimulatory effects through its steroidal saponins.

EFFECTS OF GLUCOCORTICOIDS ON METABOLISM OF AMINO ACIDS IN SMALL INTESTINE

Weaning is associated with a noticeable change from a high fat to a high carbohydrate diet (Henning, 1981). This extensive change in diet leads to major alterations in enzyme profiles and selective metabolism in the small intestine. Wu et al. (1994, 1995) discovered an induction of pyrroline-5-carboxylate synthase (P5CS) and arginase in enterocytes of 29-day-old pigs that were weaned at 21 days of age. The increased expression of these two enzymes results in the production of large amounts of citrulline from glutamine (Wu et al., 1994; Wu and Knabe 1995), as well as the synthesis of urea from ammonia (Wu, 1995), in enterocytes of post-weaning pigs. Furthermore, the weaning-associated changes in intestinal metabolism of glutamine and arginine are independent of a change in age or diet (Dugan et al., 1995). Because weaning is associated with an increase in plasma concentrations of cortisol in mammals (Henning, 1981), it was suggested (Wu et al., 1994) and subsequently demonstrated (Flynn and Wu 1997a, b; Flynn et al., 1999) that glucocorticoids play an important role in regulating the metabolism of arginine and glutamine in enterocytes. To support this view, administration of cortisol to 21-day-old suckling pigs (killed at day 29 of age) significantly increased the argininosuccinate lyase (ASL) and arginase activities, as well as the production of CO2, ornithine and proline from arginine in the cells (Flynn and Wu 1997a). Intestinal P5CS activity and the formation of citrulline from glutamine were increased in cortisol-treated pigs compared to control pigs (Flynn and Wu 1997b). The P5CS can promote the synthesis of citrulline and arginine (an essential amino acid for young pigs; Wu et al., 2004) from glutamine and glutamate in the small intestine. Effects of cortisol on metabolite production and those two enzymes induction were completely blocked by administration of RU486 which is a glucocorticoid receptor antagonist (Flynn and Wu, 1997a). Both cortisol and RU486 administration did not have any effect on ASL activity in enterocytes (Flynn and Wu, 1997a, b), and it shows that glucocorticoids stimulate the intestinal synthesis of citrulline which then can be released into the circulation. Consistent

with these findings, the release of citrulline by the small intestine is increased in post-weaning pigs (Wu et al., 1994).

Study of the effect of RU486 on arginine and glutamine metabolism in weanling and age-matched suckling pigs (Flynn and Wu, 1997b) showed that RU486 administration to weanling pigs reduced the activity of arginase and the subsequent production of ornithine from arginine. RU486 administration did not affect argininosuccinate synthase (ASS) activity, but it blocked the weaning associated increase in P5CS and ASL activities completely (Wu et al., 2000). RU486 also blocked increased production of ornithine, citrulline and CO2 from glutamine. At the molecular level, administration of RU486 did not show any effect on ASS mRNA levels, but it totally suppressed the weaning-associated increase in arginase and ASL mRNA levels. Another study (Flynn et al., 1999) showed that the intestinal expression of type-II arginase (mitochondrial enzyme) was increased in response to weaning or glucocorticoids while type-I arginase (located in cytoplasm) was still unchanged. It has been suggested that elevating concentrations of plasma cortisol increases arginase activity and glutamine metabolism in the small intestine via glucocorticoid receptor (Flynn and Wu, 1997a, b; Flynn et al., 1999).

Based on the finding that (Wu et al., 2000) glucocorticoids can increase arginase and argininosuccinate lyase (ASL) activity which in turn regulate metabolism of arginine in the gut and because yucca contains active steroidal saponins and can increase intestinal arginase activity (Kong et al., 2010), this thesis research was designed to investigate the effects of yucca alone and in combination with citrulline (immediate precursor of arginine) on growth performance of 21-day-old post weaning piglets.

CHAPTER II
IMPROVED EFFICIENCY OF MILK UTILIZATION BY SURVIVING LOW-BIRTH-WEIGHT PIGLETS

SYNOPSIS

The objective of this study was to determine the effect of piglet birth weight on preweaning BW, growth, mortality and milk utilization. Eighteen multiparous sows (Landrace X Large White) and their litters were used in this study. Piglets (n=160) were individually weighed immediately after birth (d 0) and at 7-day intervals for 35 days. On weighting days, individual milk consumption of piglets was determined using the weigh-suckle-weigh method. Piglets were classified according to their birth weight into four categories A: 0.7-1.09 kg; B: 1.10-1.49 kg; C: 1.50-1.89 kg; and D: >1.90 kg. Average daily gain during lactation was calculated. Individual mortality was recorded daily during the suckling phase. The lightest birth weight group showed the highest incidence of mortality (26% in first week). Increased birth weight resulted in heavier BW and faster daily gain during the 35 d of study ($P<0.01$). Heaviest birth weight piglets had the highest milk consumption and lowest ratio of gain to milk consumption ($P<0.01$). Piglets that successfully survived had relatively faster growth rate in each weak than the bigger ones.

Overall, results of this study indicated that low birth weight was directly related to higher incidence of mortality as well as lower absolute weight gain, even though the light birth weight piglets utilized milk more efficiently for growth than heavier piglets.

INTRODUCTION

For swine producers to regain and maintain profitability into the future, a continued emphasis must be placed on the improved efficiency of their entire production system.
One potential area to focus on in terms of its economic impact on production is piglet birth weight. A number of studies have reported associations between birth weight and economically important traits such as growth (Quiniou et al., 2002; Fix et al., 2010; Schinckel et al., 2010), efficiency (Fix et al., 2010; Schinckel et al., 2010), and survival (Quiniou et al., 2002; Fix et al., 2010).

The U.S. swine industry's emphasis on sow prolificacy has resulted in an increase in the number of live birth per sow (10.2 vs. 11.35) from 1998 to 2008 (PIGCHAMP 1998, 2008). However, increased litter size results in lower individual piglet birth weights (Roehe, 1999; Quiniou et al., 2002). Piglets with lighter birth weights continue to have lighter body weights throughout production (Powell and Aberle, 1980; Quiniou et al., 2002; Schinckel et al., 2007).

The greatest proportion of mortality in commercial pig production occurs prior to weaning. Reviews of piglet survival during lactation reported pre-weaning mortality ranging between 10 and 20% of live born pigs (Alonso-Spilsbury et al., 2007; Wu et al., 2006). Similarly, preweaning mortality was estimated at 12.8% in U.S. commercial swine herds during 2008 (PIGCHAMP, 2008). A variety of causes lead to pre-weaning mortality; one of these causes is low individual piglet birth weight (Alonso-Spilsbury et al., 2007).

Pigs with low birth weights have a greater chance of being stillborn (Quiniou et al., 2002; Zaleski and Hacker, 1993; Leenhouwers et al., 1999) or not surviving to weaning (Gardner et al., 1989; Quiniou et al., 2002). Pigs from litters with greater variation in birth weight have been reported to be more prone to pre-weaning mortality (Milligan et al., 2001, 2002). Roehe and Kalm (2000) reported a similar finding of increased pre-weaning mortality for litters with greater variation in birth weight, but also concluded individual birth weight accounted for more variation and thus, was a better predictor of pre-weaning mortality.

To our knowledge no work has been done evaluating the efficiency of milk utilization and subsequent growth rate in low birth weight piglets which have successfully survived through the preweaning period. Therefore, the objective of this study was to quantify the

effect of birth weight on daily gain, mortality rate and efficiency of milk utilization throughout lactation period.

MATERIALS AND METHODS

Animals

The experiment was carried out from August 2009 to February 2010 at the Veterinary Medical Park and Animal Science Teaching and Research Center (Department of Animal Science, Texas A&M University) using 18 multiparous sows (Landrace X Large White) and their litters. Three days prior to the expected day of parturition, sows were transferred into individual farrowing pens. The experimental protocol of this study was approved by the Texas A&M University Institutional Animal Care and Use Committee.

Housing and Management

Each sow was housed with her piglets in a farrowing pen (1.8 m X 2.5 m = 4.5 m^2 including 1.98 m^2 of plastic-coated perforated floor). Each pen had metal sidewalls and was equipped with a sow feeder (0.45 m X 0.35 m) and a nipple drinker. During their lactation, sows were fed up to 7.3 kg d, separated into two feeding periods (08:00 am and 17:00 pm). The diet contained 3.30 MCal ME/kg and 18.7% protein which met the NRC requirement for lactating sows (Mateo et al., 2008). Sows had *ad libitum* access to water during the 35 d lactation period. Ambient air temperature ranged from 22-32℃; radiant heat was provided to the litter as needed.

At birth, the number and gender of piglets born both alive and dead were recorded. Mean litter size was 8.9±1.0 piglets. Teeth were clipped and tails were docked at d 3 of age. Each piglet was also marked individually with ear notches and received an iron injection. During the whole lactation period, piglets had free access to water. They were not given creep feed during the 35 d lactation period.

Data Collection and Statistical Analysis

Eighteen litters were involved in the study. All piglets (n=160) were weighed immediately after birth and on day 7, 14, 21, 28 and 35 of the lactation period. Average daily gain was calculated. On the day of weighing, three consecutive periods were analyzed from 08:00 to 17:00. Piglets were isolated from the sow for 2 hr then nursed for 1 hr and this procedure repeated three times. Milk consumption of the piglets was estimated using weight-suckle-weight (Wu G. et al., 2000). Piglets were classified into four categories according to their birth weight. A: 0.7-1.09 kg; B: 1.10-1.49 kg; C: 1.50-1.89 kg; and D: >1.90 kg. Piglets with a birth weight of 0.7 – 1.09 kg are classified as intrauterine growth retardation (IUGR) (Wu et al., 2010). Six analyses were carried out on different measures for these 4 groups. All the analyses are based on One-Way ANOVA and the Duncan's multiple range tests. ADG, body weight and milk intake of piglets were analyzed with birth weight as a fixed effect on the given days. When the piglets died, their body weight and the time of death were recorded to calculate mortality. The data from dead piglets then were excluded from further analyses.

RESULTS

Piglets Body Weight

Body weights of each of the piglets were measured at birth, with the time at birth denoted as D0. The mean birth weight for each category was calculated. Afterwards, all weaning piglets were weighted every 7 days over 35 days of lactation. For D0, D7, D14, D21, D28 and D35, ANOVA indicated that the means of the four categories on each day differed significantly ($P<0.01$): mean D > mean C > mean B > mean A (Table 1). Mortality was highest in the lowest birth weight group especially in the first week of study (Table 2). For the first week of study, mortality rate was 26.1 percent for the lightest birth weight group vs 4.26, 1.69 and 0 percent for other groups respectively. An exponential function was used to model the constant change in the independent variable (days) with the proportional change (increase) in the dependent variable (body weight). The graph of $y = e^x$ was upward-sloping, and increased faster as x increased. The body weight had an exponential relation to the growth; therefore, the results showed that for the heaviest birth weight group, body weight increased in a decreasing way. The body weights of lighter pigs increased relatively faster but were still significantly the smallest during the 35 d of lactation (Figure 1).

Table 1. Body weight of piglets during the study

Groups of piglets	n[†]	D 0*	D 7	D 14	D 21	D 28	D 35
				BW (kg)			
A: 0.7-1.09 kg	23	0.97±0.02[d]	1.71±0.08[d]	2.72±0.20[d]	4.02±0.25[d]	5.16±0.34[d]	6.26±0.43[d]
B: 1.10-1.49 kg	47	1.29±0.01[c]	2.23±0.05[c]	3.42±0.08[c]	4.69±0.13[c]	5.95±0.19[c]	7.16±0.24[c]
C: 1.50-1.89 kg	59	1.68±0.01[b]	2.69±0.05[b]	4.16±0.09[b]	5.55±0.12[b]	6.91±0.15[b]	8.26±0.18[b]
D: >1.9 kg	31	2.08±0.07[a]	3.22±0.12[a]	4.71±0.18[a]	6.11±0.22[a]	7.49±0.27[a]	8.85±0.32[a]
P value		< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01

Data are expressed as means ± SEM. The P value represents statistical significance among BW groups for each 7 d interval.

*D 0 = Day of birth.

† Number of piglets at birth.

[a-d] Means not sharing a common superscript within a column differ (P<0.01).

Table 2. Numbers of piglets at each week interval*

Groups of piglets	n†	D(0-7)	D(7-14)	D(14-21)	D(21-28)	D(28-35)
A: 0.7-1.09 kg	23	17	16	15	15	15
B: 1.10-1.49 kg	47	45	45	45	45	45
C: 1.50-1.89 kg	59	58	58	58	58	58
D: >1.9 kg	31	31	31	31	31	31

Each column shows number of live animal in each week interval.

* D (0-7) = 7 day time intervals.

† Number of piglets at birth.

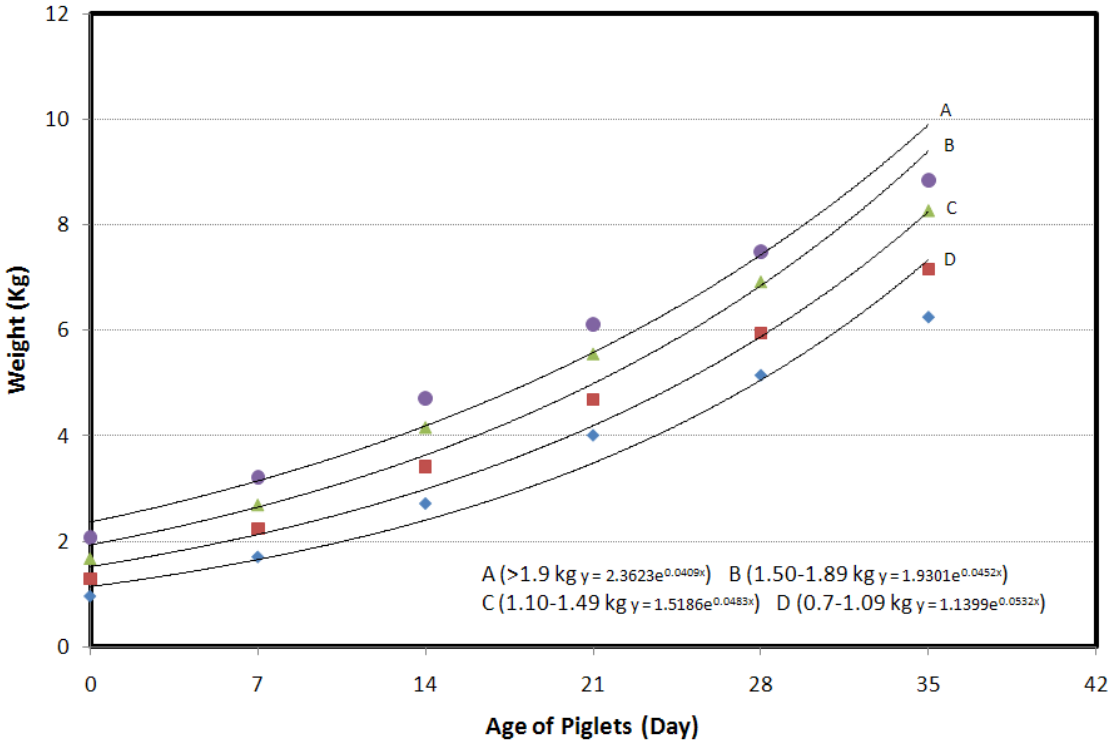

Figure 1. Body weight of piglets during the study

Percentage Increase in Body Weight

Relative growth rate of each piglet in each week was calculated based on the difference of body weight between last and first day of the week. The time intervals are denoted as D (0-7), D (7-14), D (14-21), D (21-28) and D (28-35) indicating 7 days intervals between each measurement. All ANOVA tests, each of which is for one of these five time slots, show that at least the means of two of the categories are different from each other ($P < 0.05$). For D (0-7), mean B > mean A > mean C > mean D ($P<0.01$). For D (7-14), the result is mean A = mean B = mean C > mean D with significance. And for D (14-21), D (21-28) and D (28-35), mean A > mean B > mean C > mean D (Table 3). These results indicate that the growth rate decreases at a rate proportional to initial period body weight (Figure 2). According to these results, the percentage of growth of lighter birth weight piglets was higher than their heavier contemporaries in each week if they could successfully survive during the first week of neonatal period.

Table 3. Percent increase in body weight of piglets

Groups of piglets	n†	D(0-7)	D(7-14)	D(14-21)	D(21-28)	D(28-35)
			Changes in BW (%/week)			
A: 0.7-1.09 kg	23	71.4±6.6[b]	54.7±7.2[a]	41.5±2.9[a]	28.1±1.5[a]	21.1±0.9[a]
B: 1.10-1.49 kg	47	74.9±4.2[a]	53.5±2.0[a]	37.3±2.2[b]	26.4±0.9[b]	19.9±0.5[b]
C: 1.50-1.89 kg	59	60.4±2.5[c]	54.0±1.6[a]	33.8±1.2[c]	24.6±0.8[c]	19.5±0.4[c]
D: >1.9 kg	31	54.8±3.1[d]	46.2±2.0[b]	30.1±1.4[d]	22.7±0.9[d]	18.2±0.7[d]
P value		< 0.01	< 0.01	< 0.01	< 0.01	< 0.01

Data are expressed as means ± SEM. The P value represents statistical significance among BW groups for each 7 d interval.

† Number of animals at birth.

[a-d] Means not sharing a common superscript within a column differ ($P<0.01$).

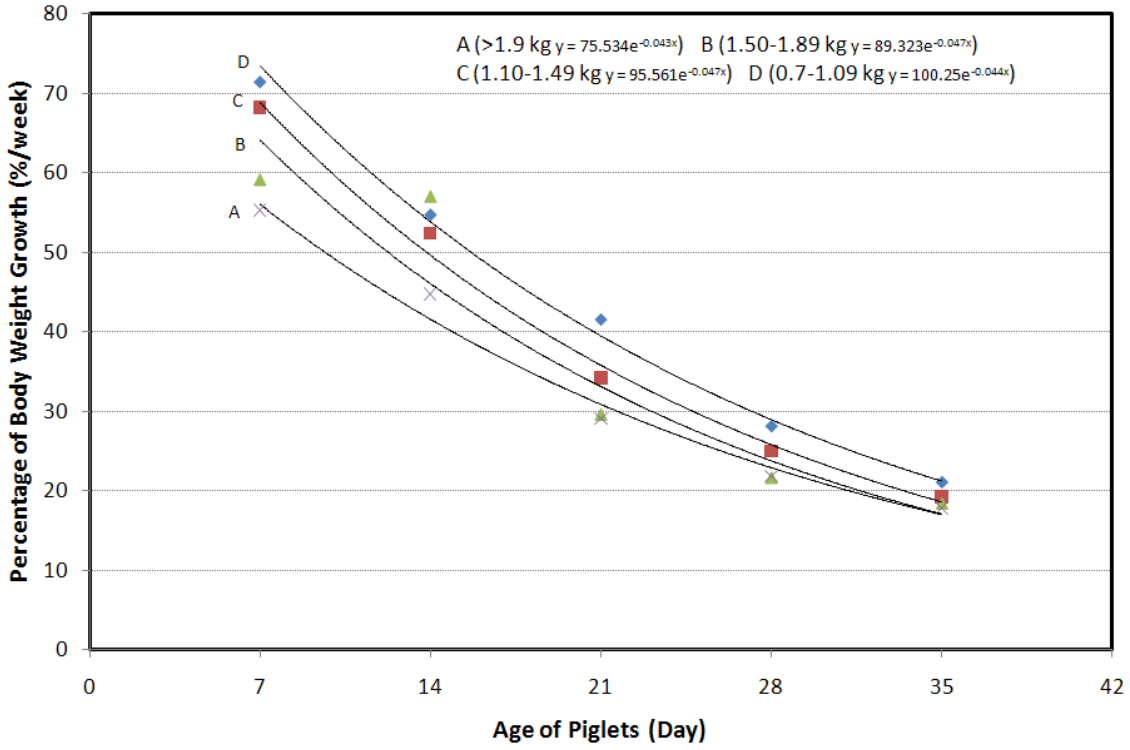

Figure 2. Growth rate of piglets measured as percentage increase in body weight in each week

Absolute Changes in Body Weight (unit: g/d)

Average daily gain (ADG) is a significant variable in assessing growth rate in animals. All ANOVA tests indicated that at least two of the means differed ($P < 0.05$) significantly for each one of the four initial weight categories. Based on the Duncan's tests, the result for D (0-7) is mean D > mean C > mean B > mean A. After week one mean D = mean C > mean B > mean A (Table 4) ($P<0.01$). Overall, the two heaviest groups were not different from each other in terms of absolute changes in body weight, but their magnitudes of changes in body weight were larger than the two comparatively lighter groups in a statistical context (Figure 3). The daily body weight gain (g/day) reached peak values for all groups between the second and third week of age and after that ADG for all groups started to decrease (Figure 4).

Table 4. Absolute changes in body weight or daily weight gain (ADG) of piglets

Groups of piglets	n†	D(0-7)	D(7-14)	D(14-21)	D(21-28)	D(28-35)
		Changes in BW (g/d)				
A: 0.7-1.09 kg	23	102 ± 10^{d}	141 ± 19^{c}	168 ± 15^{c}	163 ± 14^{c}	157 ± 14^{c}
B: 1.10-1.49 kg	47	136 ± 8^{c}	169 ± 7^{b}	182 ± 11^{b}	181 ± 9^{b}	173 ± 8^{b}
C: 1.50-1.89 kg	59	145 ± 6^{b}	209 ± 8^{a}	199 ± 7^{a}	195 ± 7^{a}	193 ± 6^{a}
D: >1.9 kg	31	163 ± 9^{a}	212 ± 10^{a}	200 ± 9^{a}	197 ± 8^{a}	194 ± 8^{a}
P value		< 0.01	< 0.01	< 0.01	< 0.01	< 0.01

Data are expressed as means ± SEM. The P value represents statistical significance among BW groups for each 7 d interval.

† Number of animals at birth.

[a-d] Means not sharing a common superscript within a column differ (P<0.01).

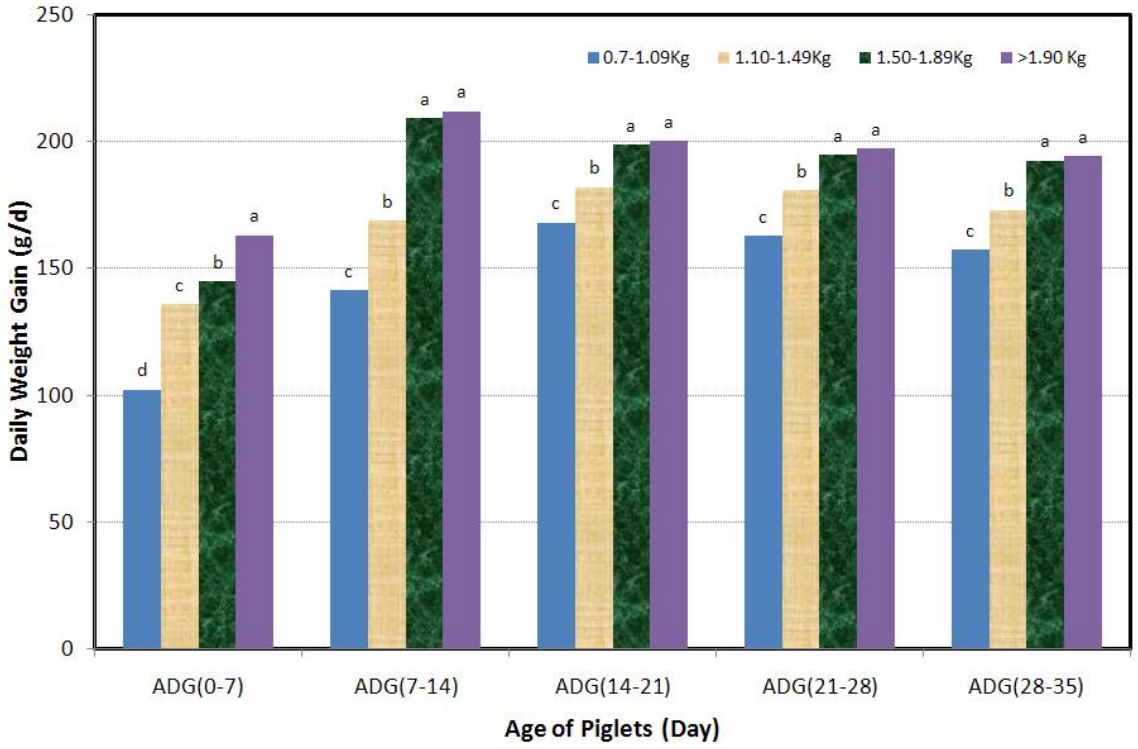

Figure 3. Comparison of average daily gain between groups

[abcd] mean not sharing a common superscript difference (P<0.01)

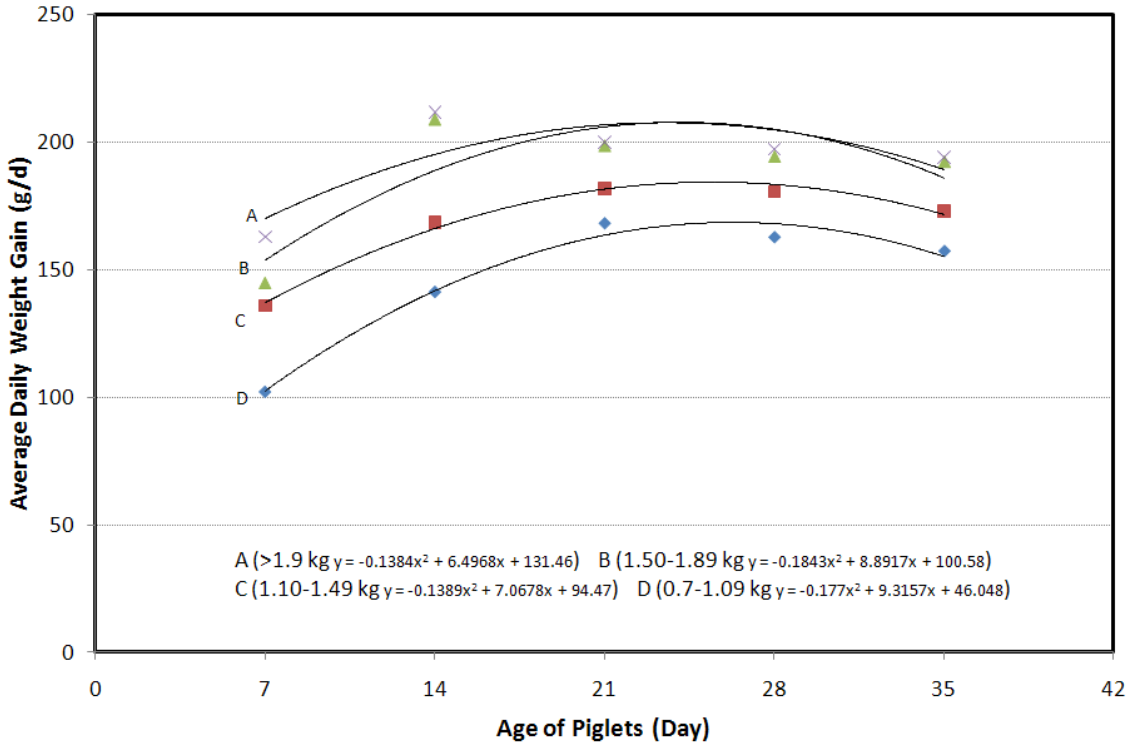

Figure 4. Average daily increase in body weight of piglets (g/day)

Milk Intake (unit: g/kg BW)

Using weight-suckle-weight technique, the average milk intake for the piglets in each category was recorded on days 7, 14, 21, 28 and 35. The milk intake then was calculated based on the total daily milk intake of the piglets and their body weight. All of the ANOVA tests indicated at least two of the means were different significantly for each one of the four categories. Based on the Duncan's test, for D7 and D14, mean D = mean C > mean B > mean A significantly. For D21, mean D > mean C > mean B = mean A with significance. For D28 and D35, mean D > mean C > mean B > mean A with significance (Table 5) ($P<0.01$). Overall, heavier piglets at birth consumed more milk per kg body weight. The highest rate of milk intake by piglets was at D7 followed by an exponential decrease over next three weeks (Figure 5). Thus, there was a limitation in milk production. As piglets grew older, their milk intake per kg body weight decreased dramatically.

Table 5. Milk consumption per kg of body weight

Groups of piglets	n†	D 7	D 14	D 21	D 28	D 35
				Milk Intake (g/kg BW)		
A: 0.7-1.09 kg	23	270±11[c]	187±8[c]	148±4[c]	120±3[d]	101±3[d]
B: 1.10-1.49 kg	47	276±7[b]	196±4[b]	150±3[c]	125±3[c]	106±3[c]
C: 1.50-1.89 kg	59	282±6[a]	210±3[a]	161±3[b]	132±2[b]	112±2[b]
D: >1.9 kg	31	284±11[a]	211±7[a]	166±6[a]	138±5[a]	119±4[a]
P value		< 0.01	< 0.01	< 0.01	< 0.01	< 0.01

Data are expressed as means ± SEM. The P value represents statistical significance among BW groups for each 7 d interval.

† Number of animals at birth.

[a-d] Means not sharing a common superscript within a column differ (P<0.01).

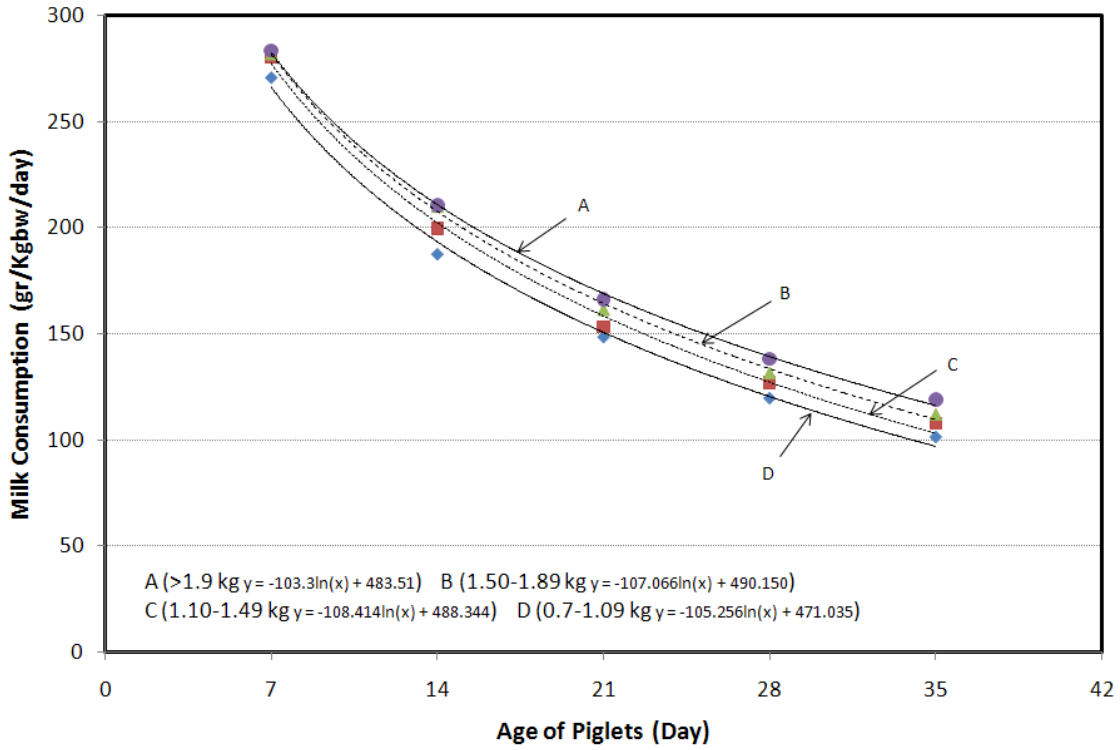

Figure 5. Milk consumption of the piglets per kg body weight for each group

Daily Milk Consumption (unit: g/d)

We recorded the average milk consumption which was measured as grams per day for individual piglets in each group on days 7, 14, 21, 28 and 35 (Table 6). All of the ANOVA

tests at least two of the means were different significantly for each one of the four groups. Based on the Duncan's test, mean D > mean C > mean B > mean A ($P<0.01$) (Table 6). As piglets became older, they consumed more milk and this increasing trend was higher in heavier piglets during the 35 d study (Figure 6).

Table 6. Milk consumption of piglets g/day/pig

Groups of piglets	n†	D 7	D 14	D 21	D 28	D 35
			Milk Intake (g/d)			
A: 0.7-1.09 kg	23	475±42^{d}	525±51^{d}	600±46^{d}	615±44^{d}	628±42^{d}
B: 1.10-1.49 kg	47	639±27^{c}	686±24^{c}	723±26^{c}	757±32^{c}	767±31^{c}
C: 1.50-1.89 kg	59	772±27^{b}	875±24^{b}	897±24^{b}	910±24^{b}	925±24^{b}
D: >1.9 kg	31	922±45^{a}	999±46^{a}	1021±45^{a}	1039±44^{a}	1055±44^{a}
P value		< 0.01	< 0.01	< 0.01	< 0.01	< 0.01

Data are expressed as means ± SEM. The P value represents statistical significance among BW groups for each 7 d interval.

† Number of animals at birth.

$^{a-d}$ Means not sharing a common superscript within a column differ ($P<0.01$).

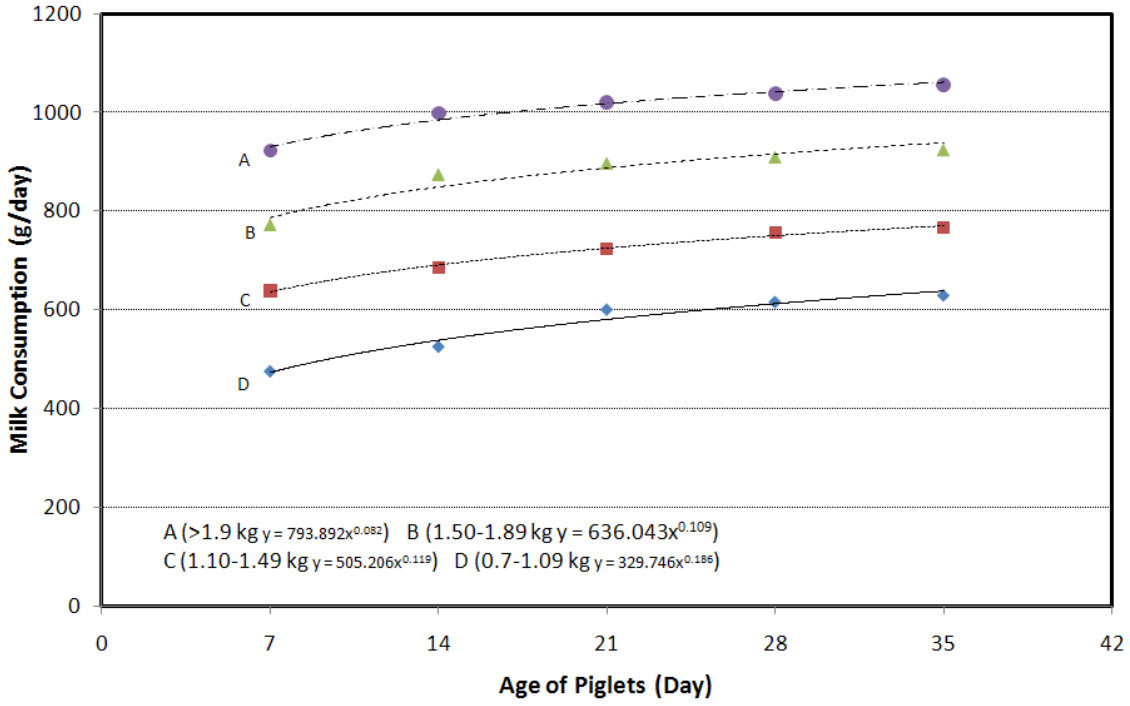

Figure 6. Daily consumption of milk by piglets

Milk Efficiency (Average daily weight gain/milk intake)

We measured the conversion of milk to body weight for the piglets in each category in five time intervals which are defined as D (0-7), D (7-14), D (14-21), D (21-28) and D (28-35). All ANOVA tests indicated that at least two of the means were different significantly for each category ($P<0.01$). The results of the Duncan's tests showed fluctuation for the first two time slots, but became quite neat and stable for the last three intervals. Specifically, for D (0-7), mean B = mean D > mean C > mean A with statistical significance. For D (7-14), mean B > mean C = mean A > mean D significantly. For the rest three time intervals, mean A > mean B > mean C > mean D with significance (Table 7).

Table 7. Efficiency of conversion of milk to body weight gain

Groups of piglets	n †	D(0-7)	D(7-14)	D(14-21)	D(21-28)	D(28-35)
		Average daily gain/milk intake; g/g				
A: 0.7-1.09 kg	23	0.184 ± 0.011^{c}	0.167 ± 0.028^{b}	0.192 ± 0.011^{a}	0.178 ± 0.009^{a}	0.167 ± 0.009^{a}
B: 1.10-1.49kg	47	0.212 ± 0.008^{a}	0.173 ± 0.007^{a}	0.168 ± 0.008^{b}	0.161 ± 0.006^{b}	0.151 ± 0.005^{b}
C: 1.50-1.89kg	59	0.206 ± 0.006^{b}	0.167 ± 0.004^{b}	0.149 ± 0.004^{c}	0.144 ± 0.004^{c}	0.140 ± 0.003^{c}
D: >1.9 kg	31	0.210 ± 0.009^{a}	0.147 ± 0.006^{c}	0.134 ± 0.006^{d}	0.130 ± 0.006^{d}	0.125 ± 0.005^{d}
P value		< 0.01	< 0.01	< 0.01	< 0.01	< 0.01

Data are expressed as means ± SEM. The P value represents statistical significance among BW groups for each 7 d interval.

† Number of animals at birth.

[a-d] Means not sharing a common superscript within a column differ (P<0.01).

DISCUSSION

Body Weight and Growth

The present study offers a new perspective on the effect of birth weight on future economically important traits (e.g., mortality and growth rate) in that it provides an analysis of birth weight as a continuous effect. In general, our findings support the previous conclusion that low-birth-weight pigs have low absolute growth rate (g/day) during the suckling period (Gondret et al., 2005; Smith et al., 2007; Bérard et al., 2008; Rehfeldt et al., 2008). Similar to these studies, pigs were weaned in the current work at an older age (28 and 35 days) than typically practiced in commercial U.S. swine production (around 21 days). Despite the use of different analyses, sample sizes, and facilities, light birth weight pigs were smaller at weaning compared to heavy birth weight pigs. Extending these reports, we noted that the relative growth rate (%/day) of surviving IUGR piglets was higher than their normal-weight counterparts (Figures 1 and 2).

Similar to the impact of birth weight on BW at weaning, regardless of weaning age, birth weight has also been shown to influence BW at various stages later in life. Dividing birth weight into categories, Powell and Aberle (1980) reported fewer days to 26 kg and 96 kg BW, Quiniou et al. (2002) reported increased BW at 63 d of age and fewer d to 105 kg, Smith et al. (2007) reported increased BW 42 d post weaning, and Rehfeldt et al. (2008) demonstrated heavier BW at 70, 133, and 180 (harvest) d of age due to greater birth weight. However, in the present study, low-birth-weight pigs that successfully survived during preweaning showed a higher rate of growth as percentage increase in each week although they did not catch up in absolute body weight (Figure 2).

While not discussed by Rehfeldt et al. (2008), it appears there was a numeric disparity in the difference between heavy vs. middle categories compared to the difference between middle vs. light categories where the difference between light vs. middle birth weight was greater than the difference in middle vs. heavy category. This would agree with the present study findings of a greater difference in future BW for the lowest birth weight pigs (Table 1). Again, using a cubic model, Schinckel et al. (2007) reported BW at 126 and 168 d of age, increased at a decreasing rate as birth weight increased, similar to our observation at day 35.

Regardless of the number of animals used, increased birth weight resulted in increased BW measured at various stages during the study period (Figure 1). However, it is important to examine differences in future BW across the birth weight distribution and realize that an increase in birth weight from 0.7 to 1.0 kg does not have the same effect as an increase from 2.0 to 2.2 kg. From these results, it is apparent that birth weight affects future BW. The major cause of this appears to be a difference in ADG. Based on results from the current study, birth weight affects ADG during all phases of production; the difference is greatest for the lightest birth weight pigs (Figure 3). The findings of differences in ADG are in agreement with Rehfeldt et al. (2008). Not only do heavier pigs begin life with an advantage in weight but pigs at the lower end of the birth weight distribution, due to reduced ADG, fall further behind in BW over time (Table 3).

Several factors, both prenatal and postnatal, are likely responsible for this decrease in future growth due to reduced birth weight. First, low-birth-weight pigs had a smaller number of muscle fibers than heavier birth weight pigs (Nissen et al., 2004; Gondret et al., 2005, 2006; Rehfeldt and Kuhn, 2006). The number of muscle fibers is determined prenatally; however, the increase in the size of the muscle fiber impacts growth (Dwyer et al., 1993; Rehfeldt et al., 2000; Herfort Pedersen et al., 2001). Additionally, rates of protein synthesis in skeletal muscle are lower in IUGR pigs than normal-birth-weight pigs during the suckling period (Junjun Wang and Guoyao Wu, unpublished data). Thus, because the growth of pigs is critically dependent on protein accretion in skeletal muscle, fewer muscle fibers in IUGR pigs would result in reduced future growth. Secondly, colostrum from the sow provides the newborn piglet with vital energy and maternal antibodies (Le Dividich et al., 2005). Several studies have reported at least a minor relationship between increased birth weight and the selection of anterior teats (McBride, 1963; Fraser, 1975; Hartsock et al., 1977) which have been shown to produce a greater amount of colostrum (Fraser and Lin, 1984) and pigs have reportedly gained more BW when nursing anterior teats (Kim et al., 2000). Other studies have measured colostrum intake and reported reduced intake due to low birth weight (Devillers et al., 2005, 2007). This difference in both colostrum and milk intake may contribute to the increase in pre-weaning ADG of pigs with heavier birth weight. The increase in ADG prior to weaning leads to heavier BW at weaning, which has been shown to result in increased post-weaning gain (Klindt, 2003). All of these factors contribute to the

reduced future BW and ADG due to reduced birth weight of piglets. However, the relationship between birth weight and growth is not linear (Figure 1). There appears to be a threshold for birth weight where once surpassed, further increase in birth weight does not result in increased BW or ADG, especially later in life.

Pre-weaning Mortality

Increased birth weight was associated with a reduced ($P < 0.01$) chance of mortality prior to weaning. The greatest impact of birth weight on pre-weaning survival was for pigs with the lowest birth weights (Table 2). These findings are in agreement with other studies (Pettigrew et al., 1986; Gardner et al., 1989; Roehe and Kalm, 2000; Quiniou et al., 2002). Increased pre-weaning mortality due to reduced birth weight could be attributable to a variety of prenatal developmental and postnatal environmental factors. Two postnatal factors which have been reported in the literature are vitality and food intake. De Roth and Downie (1976) reported lower birth weight pigs were given lower, or poorer, viability scores immediately following birth, and were more likely to suffer pre-weaning mortality. Lower birth weight pigs consume less colostrum and are more likely to suffer pre-weaning mortality (Devillers et al., 2005; Devillers et al., 2007). Other than crushing of piglets by the sow, early life mortality is presumably attributable to insufficient colostrum consumption (Le Dividich et al., 2005). While most pre-weaning mortality occurs early in lactation (Roehe and Kalm, 2000), there is also the potential for pigs to fall behind due to reduced milk consumption. Lighter birth weight pigs have been shown to be at a competitive disadvantage and subject to less milk consumption (Hartsock and Graves, 1976). Milk intake is vital to the survival of the piglet. Our results also confirmed heavier birth weight pigs consume significantly more milk ($P<0.01$) than the lighter piglets throughout study (Table 5 and Table 6). Despite the availability of creep feed, pigs are mostly dependent on the sow to meet their nutrient and energy requirements prior to weaning (Sørensen et al., 1998).

Many studies have shown increased pre-weaning mortality in older sows (Gardner et al., 1989; Roehe and Kalm, 2000; Knol et al., 2002). This could be attributable to reduced litter size on younger sows; number of fully formed pigs could be affected by parity, which may account for a portion of the variation associated with litter size. Another explanation

may be the increased farrowing duration of older parity sows described previously (Canario et al., 2006). The extended parturition of older sows could also lead to weaker pigs that survive through birth but are compromised and consequently susceptible to pre-weaning mortality. Roehe and Kalm (2000) and Rydhmer et al. (2008) showed preweaning mortality increases when gestation period decreases. Reduced gestation interval may result in less physiologically mature pigs being born and are more susceptible to pre-weaning mortality. Colostrum production has also been associated with sow age and induced litters with short gestation lengths. The reduction in colostrum production led to reduced consumption by the piglets and adversely affected pre-weaning mortality (Devillers et al., 2005; Devillers et al., 2007).

To our knowledge, no result has been previously reported regarding milk conversion ratio or the relative rate of growth in each week for low birth weight piglets that successfully survived during preweaning period. Our data showed that surviving low-birth-weight piglets are, to a large extent, more efficient in milk utilization after day 14 (Table 7) and grow relatively faster in each week (Table 3) compared heavier birth-weight piglets. One possible explanation of this novel observation could be the lower maintenance requirement of energy and protein for low-birth-weight piglets due to reduced mass of the small intestine and liver, as well as reduced rates of protein degradation and amino acid oxidation in the whole-body, when compared to their bigger littermates. Also, bigger piglets require more energy and amino acids for their maximal performance during late lactation when production of sow's milk is limited. Given the advantage of surviving IUGR piglets in utilizing milk more efficiently for BW gain during the suckling period, every effort must be made to reduce neonatal mortality particularly in the first week of postnatal life.

In conclusion, our results confirms that low birth weight piglets grow in a slower rate and have a higher preweaning mortality compared to heavier birth weight piglets. Notably, IUGR piglets that survived successfully during the preweaning period can utilize milk more efficiently than bigger ones. The findings of the present work are significant in that they provide a new database for future studies to elucidate the biochemical mechanisms responsible for enhanced efficiency of metabolic transformations in surviving IUGR piglets. We propose that newborn piglets with a birth weight greater than a surviving threshold and

with reduced variation in birth weight are likely to grow more efficiently in response to the current inadequate production of milk by sows.

CHAPTER III
DIETARY SUPPLEMENTATION WITH YUCCA ENHANCES GROWTH PERFORMANCE OF WEANLING PIGLETS FED A CITRULLINE-FORTIFIED DIET

SYNOPSIS

Two trials were conducted to determine the effects of supplementing Yucca schidigera (BIOPOWDER) alone and along with citrulline to the diet on growth performance and feed efficiency in pigs weaned at 21 d of age. A total of 111 pigs, which were offspring of Large White x Landrace females bred to Duroc sires, were used in this study. In the first trial, pigs were fed one of three diets including: 1) a corn- and soybean meal-based diet (control), 2) the basal diet supplemented with 120 ppm BIOPOWDER, and 3) basal diet supplemented with 180 ppm BIOPOWDER. Second trial was conducted as the first trial except that the basal diet contained 0.2% L-citrulline. Both trials started at d 21 of age (d 0 of study) and finished at d 42 of age (d 21 of study). Average daily gain and feed intake were recorded weekly. On the last day of both trials, blood samples were taken from the jugular vein of all pigs 2h after meal, and plasma was analyzed for free amino acids. Results of the first trial showed no difference in BW, ADG and feed intake among groups. In the second trial, BW and feed efficiency of pigs supplemented with 120 ppm BIOPOWDER plus 0.2% citrulline were higher ($P < 0.05$) than the control group. These findings indicate that supplementing 120 ppm BIOPOWDER to a citrulline-fortified diet can improve growth performance of weanling pigs.

INTRODUCTION

The *Yucca schidigera* plant is endemic of the southwest desert in the United States and the north part of Baja California in Mexico (Cheeke, 2000; Colina et al., 2001). The *Yucca schidigera* extract (BIOPOWDER) is generally recognized as a safe (GRAS) product and approved by the U.S. Food and Drug Administration (FDA) as a natural food adjuvant under Title 21CFR 172.510. This unique substance is also fed to livestock species (including swine) and poultry to improve air quality in production barns, as well as animal health and productivity.

BIOPOWDER is known to bind ammonia and reduce odors, therefore benefiting the housing environment for livestock species and poultry (Cheeke, 2000; Colina et al., 2001*)*. Thus, this substance is widely used in animal nutrition. However, as steroidal derivatives, effects of BIOPOWDER would depend on its supplemental dose. Of particular interest, through regulation of cellular signaling pathways mediated by steroid receptors (Kuhn, 2002), BIOPOWDER may stimulate expression of intestinal arginase to hydrolyze arginine into urea plus ornithine (Flynn et al., 1997). Because arginine is a nutritionally essential amino acid for young pigs (Wu et al., 2004), availability of arginine in the circulation may be a critical factor affecting the actions of BIOPOWDER on the neonates.

The objective of this study is to determine the growth performance of weanling pigs supplemented with BIOPOWDER alone and along with citrulline. Citrulline was included in the basal diet for two reasons. First, catabolism of citrulline by the small intestine of weanling pigs is limited in comparison with arginine (Flynn and Wu, 1997). Second, nearly all of citrulline is converted into arginine in pigs (Wu et al., 2009).

MATERIALS AND METHODS

All animals in this study were managed according to experimental protocols approved by the Texas A&M University Institutional Animal Care and Use Committee.

Animals, Housing and Management

This experiment was carried out in Animal Science Teaching and Research Center (Department of Animal Science, Texas A&M University). All pigs were born from Large White X Landrace females bred to Duroc sires, and were previously ear-notched for identification. Postweaning pigs were housed in 1.8 m X 2.5 m pens with plastic-coated perforated flooring. Each pen had metal sidewalls and was equipped with a 7-hole single sided nursery feeder and a nipple drinker. Air temperature was initially 30℃ and was gradually reduced to 24℃ by the end of the experiment.

Animals were fed a corn- and soybean meal-based diet (Wu et al., 1996) supplemented with 0, 120 or 180 ppm yucca schidigera powder (BIOPOWDER; provided from AGROIN, BAJA AGRO INTERNATIONAL SA. DE C.V.) and 0 or 0.2% L-citrulline (provided from AJINOMOTO CO., INC Tokyo, Japan). A total of 111 pigs weaned at 21 day of age were used in this study.

The corn and soybean meal-based diet was purchased from a local feed manufacturer (Producers Cooperative Association, Bryan TX, Product # 512) and contained 13.4 MJ ME/kg, 21% protein, 1.35% lysine, 0.9% calcium and 0.6% phosphorus. The diet was medicated (0.11 mg of chlortetracycline, 0.11 mg sulfamethazine, and 0.05 mg of penicillin per kg) and supplied in a powder form. Pigs had *ad libitum* access to water and feed during the 21 day experiment.

Experimental Design

Two trials were conducted to determine the effects of supplementing BIOPOWDER alone and along with citrulline to the diet on growth performance and feed efficiency in pigs weaned at 21 d of age. In the first trial, pigs weaned at 21 days of age were randomly assigned into one of three dietary groups: 1) a corn- and soybean meal-based diet (control) containing 13.4 MJ ME/kg and 21% protein (Wu et al., 1996); 2) the basal diet supplemented with 120 ppm BIOPOWDER; and 3) the basal diet supplemented with 180 ppm BIOPOWDER. All the diets were well mixed using a Hobart mixer machine. Piglets were housed in pens (4 to 6 pigs/pen). Pigs had free access to their diets and drinking water during

the entire experimental period. A second trial was conducted as the first trial except that the basal diet contained 0.2% L-citrulline. Both trials started at d 21 of age (d 0 of study) and finished at d 42 of age (d 21 of study). Body weights and daily weight gain of individual pigs as well as feed intake of pigs in each pen were recorded weekly. On the last day of both trials, blood samples were taken from the jugular vein of all pigs 2h after meal, and plasma was stored at -80^{o}C until analysis.

Analysis of Free Amino Acids in Plasma

Plasma samples were deproteinized by treating 40 µl of plasma with 40 µl of 1.5 M $HClO_4$. The acidic mixture was neutralized with 20 µl 2 M K_2CO_3 and diluted with 900 µl of HPLC grade water, resulting in a total dilution factor of 25. The deproteinized samples were then centrifuged at 10,000 g for 2 min and the supernatant fluid was used for the HPLC analysis, as described by Wu and Meininger (2008).

Calculation Data Analysis

All results are shown as Mean ± SEM. Data were analyzed by one-way Analysis of Variance (ANOVA), with pig as the experimental unit for data on body weight and daily weight gain and pen as the experimental unit for data on feed intake and feed efficiency. One-way ANOVA was used to test the equality of three population means for statistical significance. This analysis was done by partitioning the total variance into two components. One component was calculated based on random error, and the other one was determined on the basis of the differences among three means. The second component was then tested for statistical significance. The F-distribution was used to investigate the significance of this component. The null hypothesis that there was no significant difference between different groups of data was rejected, and the alternative hypothesis that the means were different was accepted, if the test indicated significance. When a significant treatment effect was found, Duncan's test was used to separate the means. Results were considered significant at $P<0.05$.

RESULTS

Trial 1: Effects of Dietary Supplementation With BIOPOWDER Alone

All data regarding effects of dietary supplementation with BIOPOWDER alone on body weight, average daily gain, feed intake, feed efficiency and plasma amino acids are summarized in Tables 8 and 9. During the feeding period from day 0 to day 21, feed intake or the average daily gain (ADG) of pigs fed a control basal diet or BIOPOWDER-supplemented diets did not show any difference among groups. Weekly measured body weight gains of pigs or final body weights were not significantly different among groups; although the control group had a tendency to grow faster. During the 21 day feeding period, feed efficiency did not differ among the three groups of pigs.

Dietary supplementation with 120 and 180 ppm BIOPOWDER progressively reduced ($P<0.05$) plasma concentrations of citrulline in a dose-dependent manner (Table 9). Interestingly, concentrations of all the three BCAA, aspartate, histidine, threonine, methionine, tryptophan, phenylalanine, ornithine, and lysine in plasma of pigs fed the 120 ppm BIOPOWDER group diet were higher ($P < 0.05$) compared with the control and the 180 ppm BIOPOWDER groups. Concentrations of asparagine, serine, glutamine, glycine, b-alanine, taurine, and alanine did not differ between the control and the 120 ppm BIOPOWDER groups, and values in either group were higher ($P<0.05$) than those in pigs fed the 180 ppm BIOPOWDER diet. Among all amino acids analyzed, circulating levels of arginine and glutamate were not affected by BIOPOWDER supplementation.

Table 8. Effects of dietary supplementation with BIOPOWDER alone on postweaning pigs

Variable	BIOPOWDER in the diet (ppm)			P-value
	0	120	180	
Body weight, kg				
D 0	5.45±0.25	5.62±0.19	5.45±0.23	0.83
D 7	5.70±0.27	5.69±0.21	5.61±0.24	0.96
D 14	6.85±0.38	6.78±0.31	6.46±0.32	0.69
D 21	8.44±0.51	8.01±0.42	7.81±0.39	0.60
Change in BW, g/d				
D 0-7	34±7.1	9.7±7.4	23±7.1	0.060
D 7-14	164±19	156±17	121±15	0.17
D 14-21	227±23	175±19	194±18	0.19
D 0-21	142±14	114±12	113±9	0.14
Feed intake, g/kg BW/d				
D 0-7	20.2±3.4	17.9±3.5	19.9±3.2	0.87
D 7-14	39.5±0.6	38.6±0.9	34.9±2.7	0.90
D 14-21	42.8±1.4	41.9±0.9	43.3±1.9	0.97
D 0-21	34.9±2.1	32.8±1.6	32.7±1.7	0.99
Feed Efficiency, gain/feed				
D 0-7	0.37±0.12	0.09±0.03	0.29±0.16	0.28
D 7-14	0.73±0.13	0.72±0.12	0.58±0.11	0.70
D 14-21	0.77±0.12	0.60±0.09	0.68±0.10	0.65
D 0-21	0.68±0.11	0.56±0.08	0.57±0.07	0.69

Data are means ± SEM. n = 22/group for body weight data; n = 4 pens/group for feed intake and feed efficiency.

Table 9. Concentrations of amino acids in plasma of pigs supplemented with 0, 120 ppm and 180 ppm of BIOPOWDER from d 21 to 42 postweaning

Variable	BIOPOWDER in the diet (ppm)			P-value
	0	120	180	
	nmol/ml			
ASP	18±1[b]	22±3[a]	14±1[c]	0.02
GLU	163±22	210±34	158±34	0.32
ASN	110±13[a]	130±9[a]	80±9[b]	<0.01
SER	145±8[a]	162±16[a]	103±10[b]	<0.01
GLN	608±45[a]	613±35[a]	471±42[b]	0.01
HIS	65±4[b]	78±8[a]	52±4[c]	<0.01
GLY	912±53[a]	879±185[a]	637±29[b]	<0.01
THR	182±14[b]	263±36[a]	116±9[c]	<0.01
CIT	68±5[a]	58±5[b]	39±3[c]	<0.01
ARG	132±10	135±9	123±20	0.76
b-ALA	26±1[a]	24±3[a]	15±1[b]	<0.01
TAU	49±9[a]	63±11[a]	33±4[b]	<0.01
ALA	483±44[a]	587±70[a]	356±58[b]	0.01
TYR	111±8[a]	111±6[a]	68±8[b]	<0.01
TRP	41±3[b]	54±5[a]	30±3[c]	<0.01
MET	43±4[b]	65±9[a]	36±7[b]	<0.01
VAL	132±12[b]	206±12[a]	124±13[b]	<0.01
PHE	83±6[b]	100±8[a]	69±5[c]	<0.01
ILE	80±6[b]	112±12[a]	71±7[b]	<0.01
LEU	139±10[b]	186±14[a]	123±15[b]	<0.01
ORN	113±7[b]	135±10[a]	87±8[c]	<0.01
LYS	95±16[b]	240±36[a]	100±27[b]	<0.01

Data are means ± SEM, n = 10.
a-b: Means sharing different superscripts within a row differ (P< 0.05).

Figure 7 shows final body weights were significantly different among groups during the 21 days of study. Figure 8 demonstrates that control group had a higher tendency to gain more daily weight over 21 day postweaning period.

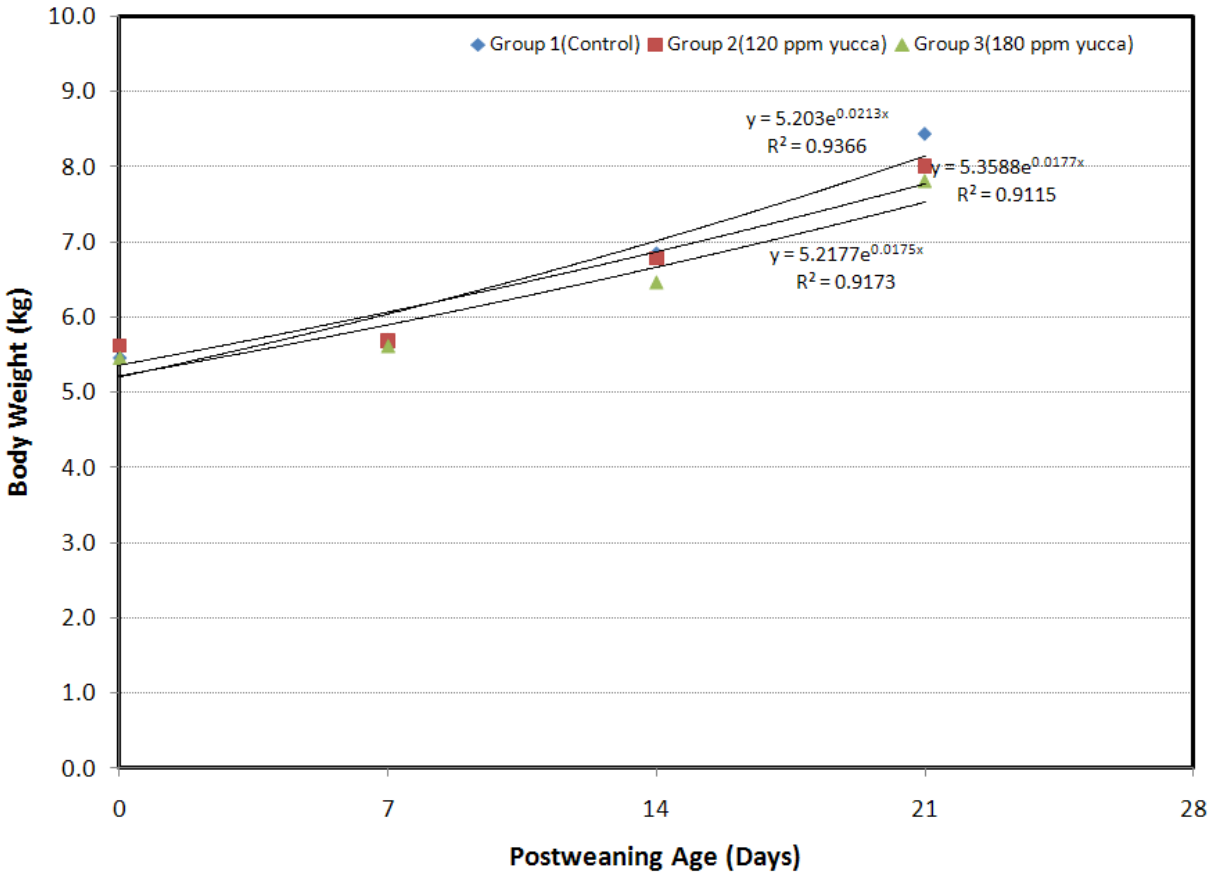

Figure 7. Body weight of pigs supplemented with 0, 120 ppm and 180 ppm BIOPOWDER in the diet from d 0 to 21 postweaning

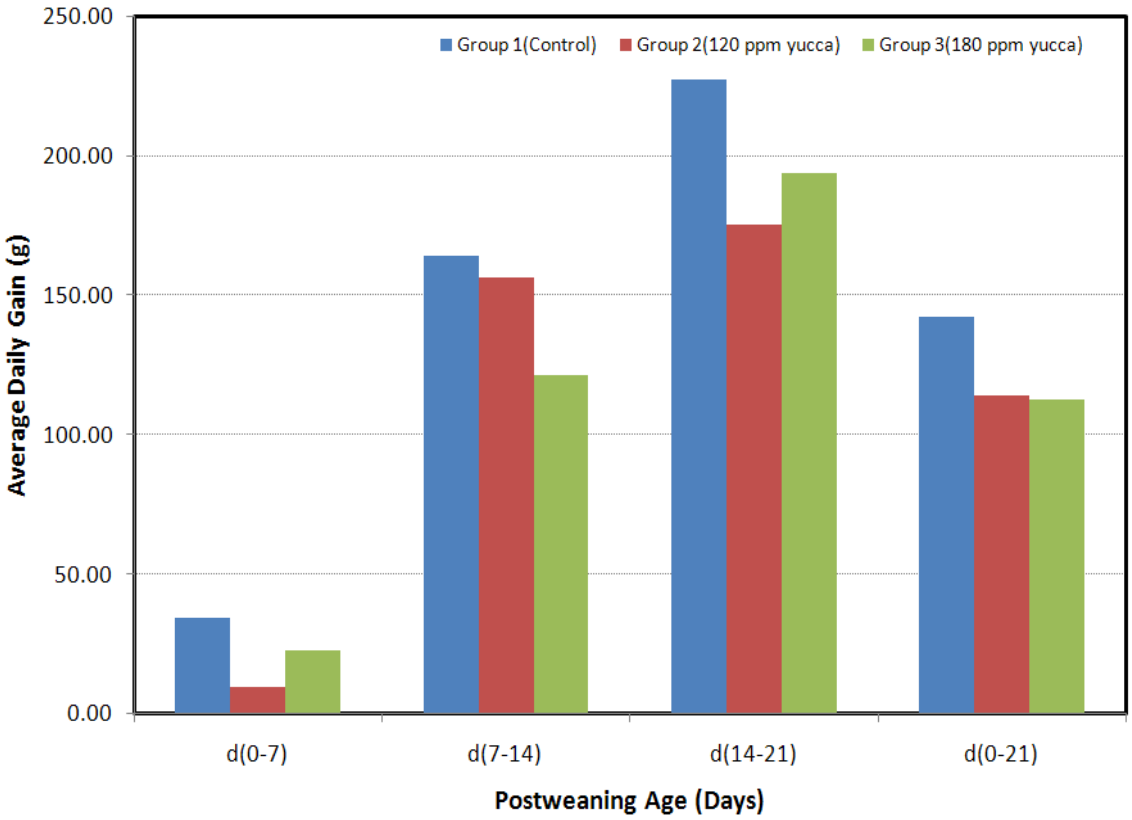

Figure 8. Average daily gain of pigs supplemented with 0, 120 ppm and 180 ppm BIOPOWDER in the diet from d 0 to 21 postweaning

Trial 2: Effects of BIOPOWDER Supplementation on Pigs Fed a Citrulline-Fortified Diet

All data regarding effects of supplementing BIOPOWDER to a citrulline-fortified diet on growth performance of pigs are summarized in Tables 10 and 11. Body weights of pigs in the first week did not differ among the three treatment groups. On d 14 and 21 postweaning, the body weights of pigs fed the 120 ppm BIOPOWDER diet were heavier ($P \leq 0.05$) than those in the control group and pigs fed the 180 ppm BIOPOWDER diet. During the first 2 weeks postweaning, feed intake did not differ among the three groups of pigs. However, in week 3, feed intake was lower ($P < 0.05$) in pigs fed the 120 ppm BIOPOWDER diet compared with the other two groups. Overall, feed efficiency was improved ($P < 0.05$) in pigs fed the 120 ppm BIOPOWDER diet than the control group.

Concentrations of the following amino acids in plasma of pigs fed the 120 ppm BIOPOWDER diet were higher ($P < 0.05$) compared with the control group: Glu, Gly, Ala, Phe, three branched-chain amino acids (BCAA), and lysine (Table 11). Except for BCAA and Lys, which exhibited higher circulating levels in pigs fed the 180 ppm BIOPOWDER diet than in the control group, concentrations of other amino acids in plasma did not differ among these two groups of pigs.

Table 10. Effects of BIOPOWDER supplementation on growth performance of pigs fed a citrulline-fortified diet

Variable	Yucca in the diet (ppm) + 0.2% Citrulline			P-value
	0	120	180	
Body weight, kg				
D 0	5.49±0.08	5.63±0.14	5.46±0.11	0.54
D 7	6.03±0.18	6.13±0.14	5.94±0.16	0.69
D 14	6.62±0.14	7.18±0.19	6.63±0.18	0.04
D 21	8.55±0.23[b]	9.52±0.22[a]	8.64±0.33[b]	0.05
Change in BW, g/d				
D 0-7	76±17	72±8	69±10	0.91
D 7-14	85±19[b]	150±12[a]	98±6[b]	<0.01
D 14-21	292±20	325±18	304±20	0.55
D 0-21	146±9[b]	186±8[a]	153±14[b]	0.058
Feed intake, g/kg BW/d				
D 0-7	31.8±3.3	28.4±3.3	30.1±2.2	0.66
D 7-14	47.0±3.0	41.6±3.0	44.0±3.0	0.59
D 14-21	49.7±1.1[c]	42.2±1.6[a]	46.7±2.1[b]	0.03
D 0-21	40.4±0.9[c]	35.1±0.5[a]	38.6±1.1[b]	<0.01
Feed efficiency, gain/feed (g/g)				
D 0-7	0.40±0.13	0.46±0.05	0.39±0.05	0.77
D 7-14	0.43±0.14	0.57±0.05	0.36±0.04	0.28
D 14-21	0.60±0.08	0.79±0.06	0.73±0.08	0.29
D 0-21	0.52±0.03[b]	0.69±0.03[a]	0.57±0.06[a]	0.04

Data are expressed as means ± SEM. n = 15/group for body weight data; n = 4 pens/group for feed intake and feed efficiency.

[a-c] Means not sharing a common superscript within a row differ (P<0.05).

Table 11. Effects of BIOPOWDER supplementation on concentrations of amino acids in plasma of pigs fed a citrulline-fortified diet from d 0 to 21 postweaning

Variable	BIOPOWDER in the diet (ppm)			P-value
	0	120	180	
	nmol/ml			
ASP	47±2	50±5	38±2	0.068
GLU	185±4[b]	300±40[a]	203±9[b]	<0.01
ASN	103±8	128±14	118±13	0.360
SER	175±11	186±16	161±7	0.355
GLN	581±36	626±61	547±37	0.493
HIS	86±4	99±9	82±5	0.165
GLY	1199±92[b]	1426±102[a]	1004±8[b]	<0.01
THR	147±17	146±20	134±8	0.815
CIT	77±3	76±7	71±5	0.865
ARG	237±13	260±7	251±7	0.459
b-ALA	18±1	23±3	30±8	0.256
TAU	75±4	76±7	69±4	0.669
ALA	478±23[b]	621±48[a]	497±42[b]	0.038
TYR	134±5	140±7	131±11	0.719
TRP	66±3	77±10	69±6	0.543
MET	67±5	67±7	58±6	0.477
VAL	207±6[c]	265±20[a]	243±18[b]	0.052
PHE	104±5[c]	131±8[a]	112±5b[c]	0.018
ILE	118±4[c]	150±9[a]	133±11[b]	0.043
LEU	154±6[c]	202±13[a]	178±10[b]	0.015
ORN	157±7	185±18	147±11	0.124
LYS	285±31[c]	417±46[a]	348±22[b]	0.049

Data are means ± SEM, n = 10.

[a-b]Means sharing different superscripts within a row differ (P< 0.05).

Figures 9 and 10 show improved final body weight and daily weight gain for second group (120 ppm BIOPOWDER) of study during 21 days postweaning.

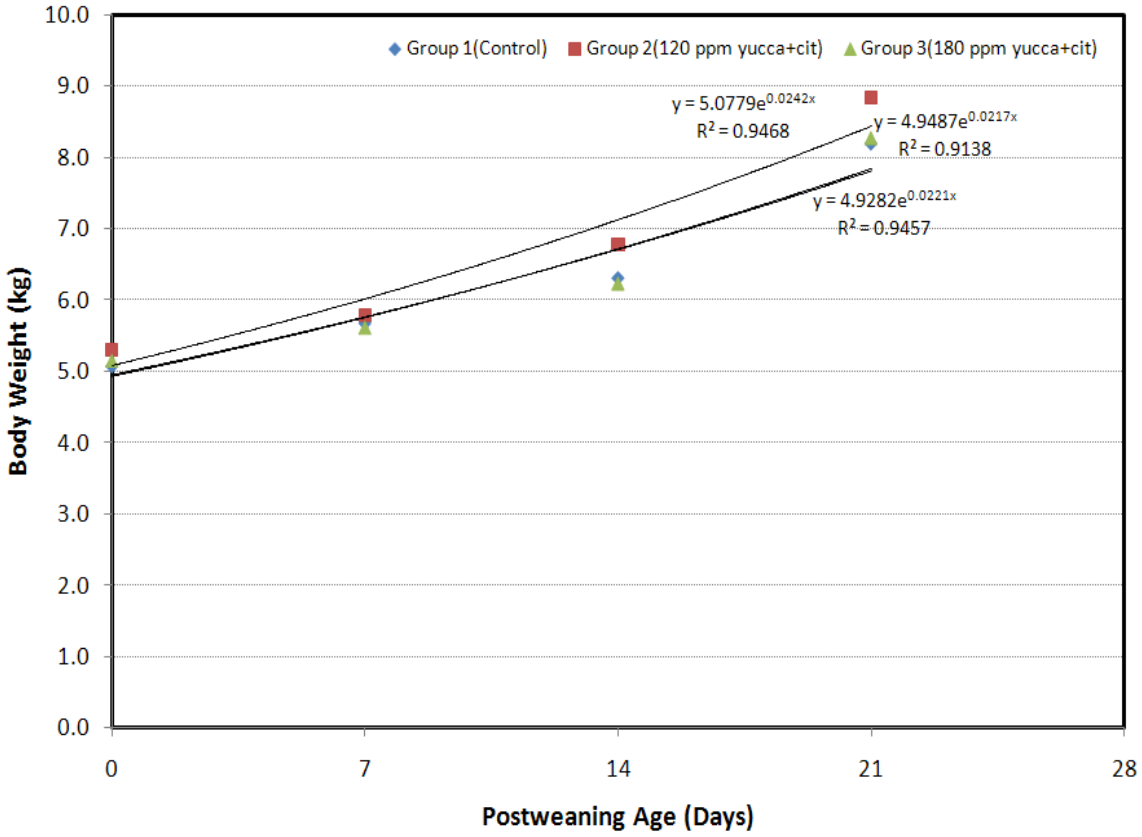

Figure 9. Body weight of pigs supplemented with 0, 120 ppm and 180 ppm BIOPOWDER along with 0.2% L-citrulline in the diet of all three groups from d 0 to 21 postweaning

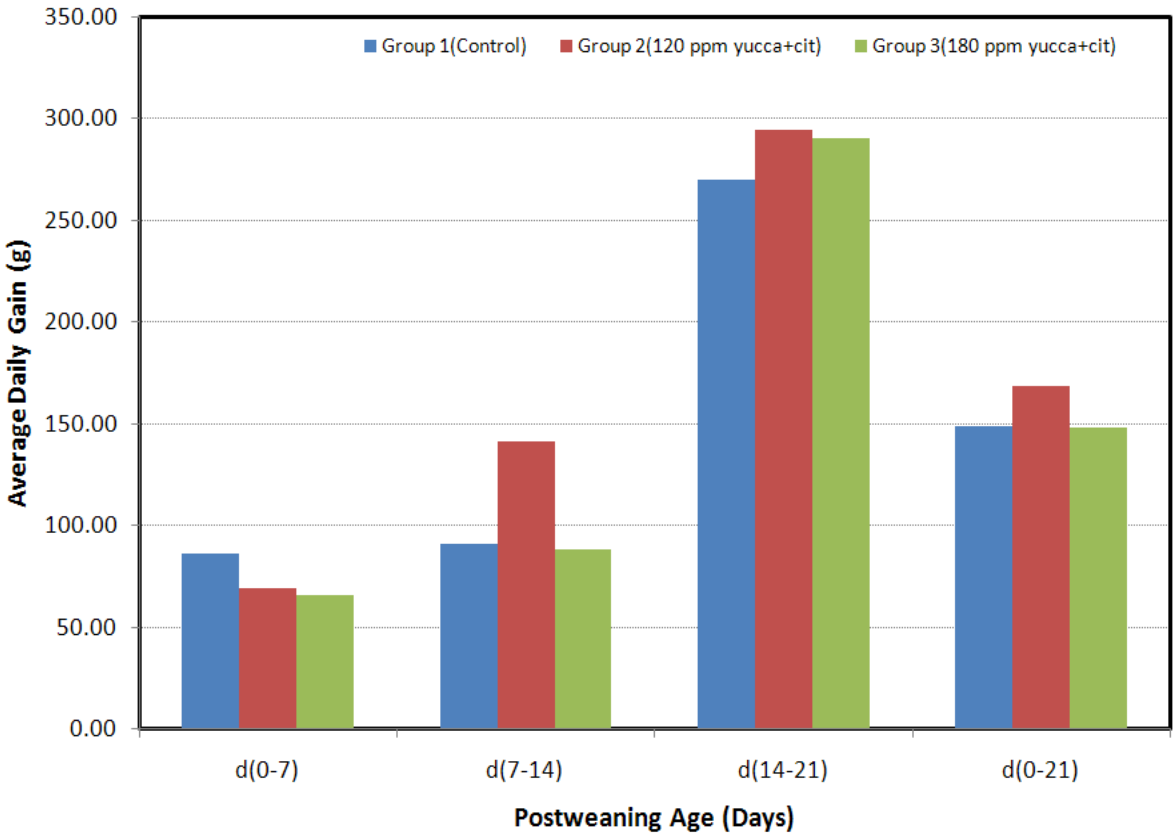

Figure 10. Average daily gain of pigs supplemented with 0, 120 ppm and 180 ppm BIOPOWDER along with 2% L-citrulline in the diet of all three groups from d 0 to 21 postweaning

DISCUSSION

Yucca powder has been successfully used in feeds to reduce ammonia emission by livestock and poultry (Cheeke, 2005). A review by Cheeke et al. (2005) listed a variety of beneficial effects of dietary supplementation with yucca extract, including reduction in the incidence of stillbirth in swine when it was fed in late gestation and enhancement in the immune function of weanling pigs. Preston et al. (1987) reported that yucca extract reduced cecal urease activity in weanling rats fed diets containing urea or extra protein. Similarly, Sutton et al. (1992) found that dietary supplementation with yucca extract decreased urease activity in swine manure. In both studies, the reduced release of ammonia from urea was interpreted as an inhibition of urease activity. However, Headon (1992) suggested that the decrease of ammonia emission by yucca extract might result, in part, from ammonia binding, because yucca extract itself did not reduce liberation of carbon dioxide from urea solution by jack bean urease. Whether it was ammonia binding or urease inhibition, the net effect of yucca extract would be a reduced level of free ammonia.

An interesting finding of the present study is that dietary supplementation with 120 ppm and 180 ppm of BIOPOWDER (a yucca extract) had no effect on growth performance or feed efficiency of postweaning pigs (Table 8). Similarly, Yen and Pond (1993) reported that dietary supplementation with yucca extract failed to enhance growth performance of young pigs. These authors suggested that a lack of a growth-stimulating effect from yucca extract could be attributed to an inability of yucca extract to exert an influence on the small intestinal mass. Additionally, Gipp et al. (1988) showed no significant effect on growth performance of weanling pigs fed 123 ppm of a different form of yucca extract. In contrast, Cromwell et al. (1985) reported, in a meeting abstract form, a tendency ($P<0.1$) for faster daily gains in weanling pigs fed diets containing 62 or 125 ppm of yucca extract.. There is not a conceivable explanation for this discrepant growth response to yucca extract between the work of Cromwell et al. (1985) and the current or other studies (Gipp et al., 1988; Yen and Pond, 1993). No assessment can be made of a possible relationship between growth performance and small intestinal mass in the studies reported by Cromwell et al. (1985) and Gipp et al. (1988), because neither group measured the small intestinal mass of pigs.

We offer our explanations for the failure of yucca extract alone to improve growth performance of weanling pigs. First, as a steroid substance, yucca extract may promote arginase expression in the small intestine and other tissues to degrade arginine (a nutritionally essential amino acid for young pigs). Second, the basal diet is inadequate in arginine, which limits tissue protein synthesis in young pigs and their growth response to yucca extract. Third, yucca extract may affect the metabolism of amino acids in a dose-dependent manner, like glucocorticoids (Flynn and Wu, 1997). This is directly supported by altered concentrations of amino acids, particularly BCAA, in the plasma of pigs supplemented with yucca alone (Table 9). Yucca, like other steroids, may inhibit BCAA degradation in cells, therefore leading to elevated levels of BCAA in plasma.

L-Citrulline is not degraded by arginase and, therefore, is effectively available for arginine synthesis by non-splanchnic bed tissues and cells. For this reason, citrulline was included in the basal diet for postweaning pigs. When arginine provision was sufficient, dietary supplementation with 120 ppm BIOPOWDER enhanced growth performance and feed efficiency in postweaning pigs. This finding indicates that an appropriate dose of BIOPOWDER can beneficially modulate metabolic pathways to improve piglet growth. Based on the actions of some steroids, we propose that a major underlying mechanism responsible for the action of BIOPOWDER may be increased protein synthesis in skeletal muscle. This hypothesis needs to be tested in future experiments.

In contrast to 120 ppm BIOPOWDER, 180 ppm BIOPOWDER did not affect growth performance of weanling pigs even though the basal diet contained supplemental citrulline (Table 10). This is due to reduced feed intake, which resulted in reduced availability of dietary amino acids for muscle protein synthesis. Also, at a higher concentration, BIOPOWDER may stimulate muscle proteolysis, as previously reported for effects of high doses of glucocorticoids on increasing this biochemical process in rat skeletal muscle, therefore attenuating an anabolic effect of BIOPOWDER on the animal. Nonetheless, 180 ppm BIOPOWDER was still effective in improving feed efficiency in postweaning pigs (Table 10).

In conclusion, dietary supplementation with BIOPOWDER alone did not affect growth performance of postweaning pigs. In contrast, supplementing an appropriate dose of this yucca extract (120 ppm) to a citrulline-fortified diet increased growth performance and

feed efficiency in these animals. Adequate availability of arginine is required for BIOPOWDER to exert its anabolic effect on piglet growth and its regulatory action on improving the efficiency of nutrient utilization in young pigs. Combining these functions of BIOPOWDER with its ammonia-binding property, this phytochemical product holds great promise for reducing ammonia emission from swine facilities worldwide.

CHAPTER IV
SUMMARY AND CONCLUSION

Birth weight has dramatic impacts on the growth of pigs from weaning till marketing. There is a threshold where an increase in birth weight does not result in improved gain. Birth weight also impacts the composition, feed intake, and efficiency of pre- and post-weaning pigs. When a pig's birth weight is greater than 1.4 kg, no additional benefit can be obtained in terms of neonatal survival, growth rate, or feed efficiency.

Results of this thesis research indicate that lighter birth weight piglets are more efficient in converting milk into weight gain. Similarly, gain to feed ratio is higher in light birth weight pigs fed a plant ingredient-based diet during the post-weaning period. However, when light birth weight pigs are given extra days required to reach a predetermined final BW, their advantage in efficiency is lost and may actually become an economically disadvantage. Low birth weight piglets grow at a slower rate and have a higher preweaning mortality compared to heavier birth weight piglets. Notably, low birth weight piglets that survive successfully during the preweaning period or that exhibit reduced variation in birth weight can utilize milk-born nutrients for growth more efficiently than bigger ones throughout the suckling period. This is important for suckling piglets because of the current inadequate production of milk by sows. Given such an advantage of surviving low birth weight piglets, every effort must be made to reduce neonatal mortality particularly in the first week of postnatal life. The findings of the present work are significant in that they provide a new database for future studies to elucidate the biochemical mechanisms responsible for enhanced efficiency of metabolic transformations in surviving IUGR piglets.

In the current U.S. swine industry, pigs are weaned usually at 21 days of age to increase sow's productivity. However, early-weaned piglets exhibit retarded growth due to stress and reduced feed intake. Thus, there is growing interest in development of new means to ameliorate the weaning-associated wasting syndrome. An important finding of this research is that postweaning growth of pigs is affected by dietary supplementation with the extract of Yucca Schidigera (BIOPOWDER) depending on the dietary availability of arginine. Yucca has been used in animal diets to reduce ammonia and stimulate growth

performance. It was previously believed that Yucca exerts its effects via its active steroidal saponins. However, dietary supplementation with BIOPOWDER alone failed to enhance weight gain in postweaning pigs. As steroidal compounds, Yucca can increase arginase activity in the small intestine to hydrolyze L-arginine (a nutritionally essential amino acid for neonates) into urea plus ornithine, thereby decreasing the entry of dietary arginine into the portal circulation. In support of this view, supplementing the basal diet with L-citrulline (the effective precursor of arginine) can be an attractive mechanism to compensate for the reduced availability of dietary arginine to extraintestinal tissues, while retaining the action of a steroid substance to beneficially regulate cellular signaling pathways and increase tissue protein synthesis. Therefore, adding 0.2% L-citrulline to the basal diet containing 120 ppm BIOPOWDER enhanced circulating levels of arginine in weanling pigs, as well as, their growth rate and feed efficiency. Future research is needed to identify the underlying mechanisms.

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