

Ractopamine for Pigs: A Review about Nutritional Requirements

Aloízio Soares Ferreira^{1,*}, Gregório Murilo de Oliveira Júnior¹, Francisco Carlos de Oliveira Silva², Rita Flávia Miranda de Oliveira¹ and Edney Pereira da Silva³

¹Animal Science Department/Departamento de Zootecnia (DZO), Universidade Federal de Viçosa (UFV), Viçosa, Minas Gerais, MG. 36571-000, Brazil

²Agriculture and Livestock Research Corporation of the State of Minas Gerais/Empresa de Pesquisa Agropecuária de Minas Gerais (EPAMIG), Viçosa, Minas Gerais, MG. 36571-000, Brazil

³Animal Science Department/Faculdade de Ciências Agrárias e Veterinárias (FCAV), Universidade Estadual Paulista (UNESP), Jaboticabal, São Paulo, SP. 36571-000, Brazil

Abstract: Heavy weight pigs tend to deposit greater quantities of fat than protein. To work around this situation, ractopamine has been used in the finishing stage. In environments with moderate temperatures, ractopamine in pig diets in the finishing phase may increase rates of weight gain and improve feed efficiency without affecting feed intake. Ractopamine increases needs of pigs in terms of lysine, phosphorus and energy. The effects of ractopamine in pigs raised under conditions of heat stress have been observed in weight gain, feed efficiency and muscle deposition rate, but not on reducing the amount of fat in pigs weighing between 95.0 and 120.0 kg. Ractopamine has promoted the increase in quantity of meat on the carcass, without altering flavor and tenderness. The weight of some organs is affected by the use of ractopamine, especially in animals under conditions of heat stress. There is need for more research relating to the effects of ractopamine with the welfare of pigs with at least 95.0 kg.

Keywords: β -adrenergic, finishing stage, lysine, phosphorus, thermal stress.

INTRODUCTION

Consumers of pork have demanded a higher quality product with less fat. Slaughterhouses, in order to increase industrial output, have preferred to process heavier pigs (between 115.0 and 130.0 kg). To match end user demand with supply of meat from the slaughterhouses, it has been proposed to use ractopamine in pig diets in the finishing phase (from 95.0 to 120.0 kg) while removing it from the diets at least ten days prior to slaughter [1-3].

The use of ractopamine in pig diets has been allowed in Brazil since 1996 and is used to improve performance and production of livestock pork, as well as increase carcass quality. Consumers of pork benefit from the use of ractopamine indirectly by purchasing a higher quality product while the pig farmers benefit since they can increase the amount of meat produced and profit from the bonus rates paid by slaughterhouses, as well as the more efficient utilization of nutrients.

Ractopamine may act in the animal metabolism by reducing deposition of fat and increasing muscle tissue, and this results in slaughter of heavier animals (weighing between 125.0 and 130.0 kg) with carcasses

equal those of the lightweight animals slaughtered (weighing between 105.0 and 110.0 kg). Moreover, because deposition of fat increases continuously with age and more food is consumed per gram of fat deposited than per gram of protein deposited, with the use of ractopamine there may be improve in feed efficiency [4].

The protein deposit rate is directly related to increased demand for lysine, therefore ractopamine may alter the needs of this amino acid and other essential amino acids in pigs since there is a direct relationship between lysine and other amino acids for maximum protein deposit in the body of the animal [5, 6]. Supplementing the diet with higher levels of lysine may alter production responses of pigs subjected to diets with ractopamine, especially early in the administration of β -adrenergic (up to 14 days) when the responses are more evident [6-8]. Additionally, the responses of animals fed diets with ractopamine can be modified according to the period and dose used [6].

Use of ractopamine to improve animal performance also demands larger quantities of other nutrients in the diet that participate in protein metabolism [9]. There is evidence that this β -adrenergic has resulted in greater muscle tissue deposits but with lower bone mass deposits and this may be due to lack of calcium and especially phosphorus to increase muscle growth without bone loss [10], but little attention has been paid to this fact [2].

*Address correspondence to this author at the Animal Science Department/Departamento de Zootecnia (DZO), Universidade Federal de Viçosa (UFV), Viçosa, Minas Gerais, MG. 36571-000, Brazil; Tel: +55-31-3899-3290; Fax: + 55-31-38991236; E-mail: gregzootec@yahoo.com.br

It has also been shown that the addition of exogenous phytase in the diet may reverse the negative effects of diets with reduced levels of available phosphorus, and therefore ensure the performance of animals due to constant release of phytic phosphorus [11]. Thus, there appears to be a dependence on lysine and other amino acids, as well as phosphorus to maximize the use of ractopamine. The potential of other factors related to the needs of these nutrients for animals also affects the use of ractopamine, where temperature may be one of these factors.

Pigs are warm-blooded animals and sensitive to environmental temperatures, especially when adults. Temperatures greater than 25°C have been considered critical for finishing pigs and there has also been reports correlating temperature with metabolic alterations and body weight of the animals, as well as feed intake [8]. Thus, if the presence of ractopamine in the diet of animals in high temperature environments also contributes to reduced feed intake, its use may be impractical, given that increased body temperature already contributes to reduced feed intake.

Based on these facts, the present analysis is presented to make suggestions for further research and use of ractopamine.

THEORETICAL REFERENCE

Ractopamine is a β -adrenergic agonist of phenethylamine group, with structure similar to the catecholamines, epinephrine and norepinephrine, and is an exogenous substance that alters the animal metabolism and distribution of nutrients favoring muscle deposition in relation to fat deposition [5, 12]. Most mammals have adipose tissue with β -receptors, which when activated by catecholamines promote lipolysis and thus reduce body fat.

According to researchers [13], the muscle tissues also possess β -adrenergic receptors that promote specific muscle actions. When agonists bind to specific receptors on the cell membrane, there is a change in receptor conformation. This mechanism permits that the receptor agonist, which is associated with G protein, binds to it and causes a change in its conformation to form a complex with the α subunit transporter of the G protein (GTP). GTP interacts with adenylate cyclase, forming the complex which converts adenosine triphosphate (ATP) to cyclic adenosine monophosphate (cAMP) [14].

The β_1 and β_2 type receptors, encountered in the β -adrenergic receptor, stimulate the adenyl cyclase system and promote increased production of cAMP. This, in turn, promotes activation of protein kinases that phosphorylate and modify the activity of several enzymes, modulating metabolic processes such as muscle contraction, stimulation of lipolysis, increased glyconeogenesis, glycogenolysis, insulin and glucagon increases, and cardiac contractions [14].

Additionally, activity of this agonist is related to the modulation of enzymes involved in the lipid and glucose metabolism [15]. Protein kinases activate the hormone-sensitive lipase enzyme that acts directly on breakdown of triglycerides, inhibition of lipogenesis *via* phosphorylation and reduced glucose transport, inactivation of acetyl-Co A carboxylase and reduced gene expression for synthesis of lysogenic enzymes (citrate lyase, malic enzyme and glucose 6-phosphate dehydrogenase). As a result there is increased catabolism of lipids *via* lipolysis and reduced biosynthesis of fatty acids and triglycerides [16, 17].

In pigs, ractopamine acts by inhibiting the binding of insulin to adipocyte adrenergic receptor, thereby antagonizing its action and consequently decreasing the synthesis and deposit of fat. It can also bind to membrane receptors and trigger a series of events that lead to increase in diameter of muscle fibers, more specifically white and intermediate fibers [18].

The main action mechanism of ractopamine has been on adipose cells with reduced synthesis and deposit of subcutaneous fat by partial inhibition of lipogenesis, which allows for increased protein synthesis and improved quantitative characteristics of pig carcasses [19-21]. However, it has been found that these effects of ractopamine are partial and temporary on blocking of lipogenesis and become evident in heavier animals, where deposit of lipids in the carcass increases at a faster rate when compared to protein [5].

Therefore, β -adrenergic additives are among the most widely used nutritional alternatives in animal production for redirection of nutrients to muscle tissue deposition at the expense of fat deposition, improving carcass traits, nitrogen retention and growth rates in animals weighting more than 95.0 kg [22, 23].

DATA FOR META-ANALYTIC STUDY

A database was used to perform a meta-analysis which was used to aid in discussions of the review. This

meta-analysis was comprise of 20 scientific technical articles published between 2007 and 2013 and the main criteria for selection of publications were (a) addition of ractopamine in the diet, (b) enviroment temperature where the trials were conducted, (c) pigs in finishing phase and (d) trials that included carcass characteristics. The methodology for the definition of dependent and independent variables and to coding of the data followed the propositions described in the literature [24] Was realized Analyses of variance-covariance which were evaluated by using of static analysis using SAS package version 9.2 (2008).

Ractopamine and Nutritional Needs of Lysine and Energy

Utilization of ractopamine may be more efficient with increased intake of essential amino acids, since there is no use in having β -adrenergic agonist if there is no retention of lysine and other essential amino acids to enable greater nitrogen retention in the muscles [5, 6]. Increased levels of lysine in the diet has changed the productive responses in pigs fed diets with ractopamina (Table 1), especially early in the administration of the β -adrenergic agonist when the responses are more evident [5, 7, 8].

As can be seen, there is an effect of temperature on the efficiency of utilization of dietary lysine. Although the amounts of lysine for maintenance are not changed, the amounts lysine for growth is greatest when levels of ractopamine are increased.

Pigs fed diets containing ractopamine and greater concentrations of lysine increased protein deposition and altered the ratio of lysine to other essential amino acids [19, 25]. On the other hand, has been reported [4] that the lysine level of 0.87% was not sufficient to meet the potential growth of animals receiving ractopamine in the diet and these researchers also

suggested that weight gain of animals was limited due to lack of nutritional adjustments between dietary amino acids, since only the level of lysine and other no essential amino acid was increased. When studying the effect of lysine supplementation and ractopamine in diets, observed a thinner layer of back fat when the lysine level was increased despite not having adjusted amino acid concentrations [20].

In contrast, hypothesized that excess lysine may limit the benefits generated by the β -adrenergic agonist by providing greater competition for absorption sites and catabolism of excess amino acids at the expense of increased protein synthesis [26]. However, researchers reported that animals receiving diets containing ractopamine with greater concentrations of lysine and other amino acids consumed more food, gained more weight and presented greater gains than animals that did not receive ractopamine in their diets [26], contrary to what was conjectured by another studies [5, 7].

In addition to the protein density, it appears that higher energy levels also favor the quantity and percentage of meat on the carcass as demonstrated in research [5, 7] that reported that the energy level can be altered with the use of ractopamine in the diet, but nevertheless, protein and amino acid needs appear to be more related to the effects of ractopamine than energy itself. According with studies [6] the relationship of energy with performance of pigs fed diets containing ractopamine is still controversial, but that the lysine:energy ratio of diets may affect weight gain and feed efficiency.

Thus, it is likely that the actions mediated by ractopamine alter amino acid requirements, especially lysine content in diets with corresponding increases for other essential amino acids, and metabolizable energy needs should be corrected to maintain the same

Table 1: Lysine Intake for Maintenance and Growth and Weight Gain in Function of Ractopamine Levels

Variables	Ractopamine levels (ppm)					CV (%)	Valor P		
	0	5	10	15	20		R ¹	T ²	R*T ³
Lysine intake, g/dia									
Maintenance	0,941	0,988	0,917	0,957	0,869	0,46	0,68	0,10	0,96
Growth	26,9	27,2	27,3	28,9	25,1	3,88	0,14	<,0001	0,79
ADG, kg ⁴	0,983	1,156	0,981	1,07	0,981	6,2	0,20	<,0001	0,35

¹R, effect of ractopamina level;

²T, effect of temperature environmental; and

³R*T, interaction of ractopamine versus temperature, and

⁴Average daily weight gain.

relationships as found in diets without ractopamine and with normal levels of lysine.

Ractopamine and Phosphorus Requirements

Considering that $\beta 1$ and $\beta 2$ type receptors stimulate the adenylyl cyclase system which increases the production of "cAMP" to promote activation of protein kinases which, in turn, "phosphorylate" and modify the activity of several enzymes that modulate metabolic processes resulting from the use of ractopamine, it must be assumed that there occurs mobilization of significant amounts of phosphorus in the animal organism with the use of ractopamine.

Evaluating the addition of 20ppm of ractopamine and different levels of phosphorus to the diets of finishing pigs, it was found that weight gain, feed intake and feed efficiency increased linearly with increased levels of available phosphorus in the diets [10]. These researchers also found that greater quantities of available phosphorus are necessary to maintain the same bone mineral content (75 g between 70.0 and 114.0 kg) to ensure the effects of ractopamine, especially in the first week of supplementation with the additive. The most likely explanation for this was that higher rates of muscle tissue growth in animals fed diets with ractopamine demanded greater phosphorus concentrations, which was initially mobilized from the bones and later turnover to these tissues.

Other attempts to demonstrate the importance of phosphorus on the effects of ractopamine have been made, but the results have not been sufficient to prove the phosphorus/ractopamine ratio. However, these attempts have been made with animals beginning in the growth stage and when utilizing low levels of ractopamine. There is evidence that levels below 20 ppm may not allow expression of the effects of ractopamine [22]. Evaluating increased levels of ractopamine (0, 5, 10 and 15 ppm) in diets for gilts, researchers verified that weight gain of the animals was not affected by the inclusion of ractopamine and these authors worked with pigs beginning in the growth phase [3].

Another additive that should be taken into consideration regarding the use of ractopamine is phytase because it acts on the availability of some nutrients, principally phytic phosphorus from plant sources. However, it should be noted that according to the theory that supports the use of ractopamine; various nutrients are integrated in process of nutrient distribution in muscle and adipose tissues. Perhaps for

this reason, researchers observed effects of phytase on the availability of phosphorus, but observed no effect of ractopamine in the diets of finishing pigs [2, 22, 27-29]. Some of these researchers worked with animals weighing less than ideal and others with insufficient amounts of ractopamine, and they did not notice the need for supplementation of the diets with lysine and other amino acids, or the need for corrections of energy values.

The integrated participation of nutrients in action of ractopamine becomes more evident when one considers, for example, that when evaluating the addition of ractopamine (only 5 ppm) plus phytase in diets with higher levels of protein and essential amino acids and greater amounts of calcium and available phosphorus for finishing animals, observed that animals fed diets containing ractopamine plus phytase, although showing no significant differences between treatments, gained 6.9% more weight, showed a 8.9% better feed conversion and weighed 2.7% more than the animals in the control treatment [11].

Thus it is clear that diets for finishing pigs weighing at least 95.0 kg, with adequate levels of amino acids and energy and with higher levels of available phosphorus may benefit from the use of ractopamine.

Ractopamine and Thermal Environment

Pigs are warm-blooded animals and therefore sensitive to environmental temperatures, especially when adults. Thus, in environments of thermal comfort, the use of ractopamine may be promoted since the animals can express their full genetic potential, with better performance and utilization of nutrients without significant alterations in feed intake. However, in high temperature environments the animals may undergo changes in their metabolism and potential for growth may be reduced, as well as alterations in food intake in an attempt to reduce the heat generated by the digestion of nutrients in the diets. In hot environments the production of thyroid hormones is probably influenced by temperature and this can affect weight gain of the animal [30], as shown in Table 1 by ADG, the which is directly related to the intake of dietary lysine.

The metabolic changes produced by ractopamine seem depend on the lysine intake and for tjis, to affect weight gain, increasing it in the animals receiving β -adrenergic agonist in their diet even though feed intake is not always influenced. Although the presence of

ractopamine may not alter feed intake, it has improved the efficiency of nutrient utilization by animals and thus significantly improved weight gain. This improvement appears to be related to increased protein deposition rates in animals compared to fat deposition, since protein synthesis adds about 35.0% water [31], and this has been considered one of the factors leading to better results for both weight gain and feed efficiency in animals fed ractopamine [4]. Therefore, there is a positive correlation between protein gain and feed conversion, indicating that pigs with high rates of muscle tissue gains present better feed efficiency [32], but there direct effect of temperature upon to ADG.

However, not only does it appear that ractopamine improves weight gain and feed efficiency, but also promotes changes in proportions of gain between fat and protein; it has also been observed that it changes the efficiency of nutrient utilization. It is possible that the changes generated by ractopamine in relation to gain can change the pathways of energy expenditures [19]. Thus, the energy savings due to better efficiency of nutrient utilization can also improve animal performance (see papers 12 and 33). In addition, energy requirements of animals that consume ractopamine can be modified, since part of energy that would be used to deposit fat is available for other metabolic functions, such as production.

Under conditions of heat stress, a reduction in basal metabolism has been reported in an attempt to reduce the generation of body heat and this occurs, among other reasons, at the detriment of lower feed intake or at the expense of productivity [33]. One cannot infer that the inclusion of ractopamine in the diet has specific actions on the control of voluntary feed intake in pigs in heat-stress environments [8, 34, 35] because in their experiments food intake did not differ between diets with or without ractopamine; however, it should be noted that these researchers worked with pigs in the growth phase and, as shown in the theoretical foundation of the effects of ractopamine in the animal organism, so these results corroborate with another researchers, where the effects of ractopamine and body heat become more evident in heavier animals (over 95.0 kg) [5].

It can thus be inferred that if nutrients such as lysine and essential amino acids, phosphorus, calcium, energy and others are not properly supplemented, feed intake of animals subjected to high temperatures tends to be less than in environments with comfort temperatures and if ractopamine further decreases

intake as a result of metabolic changes, utilization of ractopamine may be unviable for pigs under conditions of heat stress. Had been found that pigs exposed to high temperature environments significantly reduced (about 46.0%) feed intake to reduce total production of body heat [36]. Besides the effect of temperature on possible changes in feed intake of animal, energy density of feed may be another factor influencing intake. Variations in feed intake may also occur with low energy density diets since animals tend to increase feed intake to meet their energy needs [37].

However, according to studies had been observed that in environments of heat stress, the presence of ractopamine in the diet with high energy levels caused a reduction in back-fat thickness and increased the percentage of meat compared to the diet without ractopamina [8]. This fact may indicate that with nutritional corrections ractopamine in pigs can be used in the final stages of completion, even in environments of heat stress.

Improvements in feed efficiency along with improvements in weight gain of animals have been more consistent in responses regarding the use of ractopamine in diets for finishing pigs. These would be the greatest benefits for the animals fed ractopamine compared with those who not receiving the additive [23, 37] and these authors also reported that if the diets of pigs in environments of heat stress are properly corrected with phosphorus, lysine and other amino acids to acquire the adequate metabolizable lysine/energy ratio, both weight gain and feed conversion will be positively affected, as well as carcass traits. In heat stress environments when studying the inclusion of ractopamine in the diet, observed an improvement in weight gain and feed efficiency [8, 34, 35].

Just as in some experiments with pigs in conditions of heat stress the effects of ractopamine have not verified, its effects have not been observed in various experiments performed in thermoneutral environments. Evaluating doses of 20 ppm of ractopamine for pigs at ambient temperatures between 18° to 25°C, researchers observed no effect of ractopamine addition on feed intake [2, 4, 5, 12, 26, 39]. Some authors have even verified that the inclusion of ractopamine in pig diets in an environment of moderate temperatures, between 16 and 25°C, allowed a reduction in food intake of approximately 7.3% [18] and 12.9% [3]. However, these researchers paid no attention to the

details of dietary nutritional corrections or to the initial weights of the animals.

On the other hand, other researchers when assessing animals in the growing and finishing stages in thermoneutral environments have observed increases in weight gains of approximately 168 g/day or 12.2% [4] and 250 g/day or 31.3% [12] in animals fed diets with ractopamine, from the growth phase until finishing.

Most studies with ractopamine have been performed in distinct environments and environmental conditions, but worked with animals of the same species and same weight in two experiments (in an environment of heat stress and another thermoneutral) and verified that the final weights of the animals maintained in conditions of heat stress fed diets containing 20 ppm of ractopamine were lower than those of animals kept in thermoneutral environments [12, 34]. However, in both cases the final weights of the animals increased in greater proportions in the thermoneutral environment than in the heat stress environment, since differences between initial weight and final weight were 80.7% in the diets without ractopamine and 86.6% in diets with 20 ppm of ractopamine in the stressful environment, and 91.3% in the diets without ractopamine and 98.3% in diets with 20 ppm of ractopamine in the thermoneutral environment.

Thus, it can be inferred that although ractopamine improves the performance of animals maintained in hot environments, the results appear to be inferior to those obtained in animals in environments of comfort, but in both conditions with properly supplemented diets the effects of ractopamine are observed.

Ractopamine and Welfare

It has been hypothesized that ractopamine by changing the physiological conditions of pigs can cause behaviors incompatible with their welfare. For stressful conditions can lead to muscle exhaustion due to increased concentrations of degraded lactic acid as from the muscle glycogen. Moreover, in situations of fear or excitement, rapid glycogenolysis can also occur in response to the release of catecholamines and the increased activity of enzymes such as creatine phosphokinase (CPK). The release of CPK in muscle can cause prolonged recumbence and even muscle injuries. In pigs fed diets containing ractopamine has been a reported positive correlation between skin

lesions and lactate levels in blood plasma [40]. Because ractopamine is a catecholamine that also acts in glycogenolysis, it can increase the activity of CPK.

Thus, it is possible to infer that the levels of CPK, lactic acid, adrenaline, noradrenalin and cortisol, as well as visual assessments of skin lesions and behavior (frequency and time stay lying) may be parameters for evaluation of conditions tiredness and stress in pigs, in particular, fed ractopamine. However there is controversy about the effects harmful of ractopamine on animal welfare, because the amounts used in the feeding of finishing pigs is small and has not been found residues in tissues of the animal's body. Furthermore, it should be noted here that the quantities become proportionally even smaller and less available if the ractopamine is properly used in animals with weights higher the 95.0 kg.

In 1992, study using up to 15 ppm of ractopamine in pigs diets for up to six weeks from 64,0 kg, verified small effects of ractopamine on the stereotyped behavior and aggressive and these researchers inferred that the more time spent lying by animals than remained on ractopamine treatment wasn't responsible for marked changes in the behavior of pigs [41]. In 2010, one study using up to 10 ppm of ractopamine in diets for pigs from 90.0 to 107.0 kg in conditions of commercial production, observed improvements in performance and carcass quality and found no effects on the behaviour, number of skin lesions and carcass after transport [42]. These researchers also found no changes in cortisol amounts and lactate concentrations, but they found differences in CFK concentrations showing physiological changes in animals. More recently, in 2011 making use of up to 20 ppm ractopamine for 21 days in the feeding of the pigs of 87.0 to 110.0 kg found no changes in animal behavior (time lying, on standing and drinking or feeding), in heart and respiratory frequency, blood pressure and nor in the concentrations of Na and K in plasma, but they verified differences in relation to lactate concentrations (118 mg/dl x 151 mg/dl) [43].

On the other hand the use of 5 ppm or 10 ppm of ractopamine for pigs for 14 or 28 days as from 77.0 kg has detected found that lesions in the hooves of animals and no found differences between diets with and without ractopamine with relation to norepinephrine, epinephrine, dopamine, 3-4-dihydroxyphenylacetic acid, homovanillic acid, serotonin and 5-hydroxyindoleacetic acid concentrations and dopamine turnover [44, 45]. But

these researchers suggested that the aggressive pattern observed in gilts is likely linked to brain monoamine profiling of a deficient serotonergic signaling, indicated by reduced serotonin concentrations in the raphe nuclei and frontal cortex, reducing the 5-hydroxyindoleacetic acid concentrations in the amygdala, and with an enhanced dopamine release ratio in the amygdala, brain areas vital for aggression regulation.

Again, we highlight that by the theory exposed in this review to ractopamine should be used in animals with at least 95.0 kg. For if the ractopamine is not acting as a nutrients divider in the animal body, it can be a precursor to undesirable reactions in the animal organism and produce undesirable behavior in terms of welfare.

Thus, there is a need for more research relating to the effects of ractopamine with the welfare of pigs of at least 95.0 kg.

Ractopamine, Carcass Traits and Meat Quality

The principal action mechanisms of ractopamine have been on adipose cells with reduced synthesis and deposition of subcutaneous fat by the partial inhibition of lipogenesis, which allows for increased protein synthesis and quantitative improvements in carcass characteristics of the pigs [19, 21]. But, the presence of membrane receptors also leads to increase in diameter of muscle fibers, including the white and intermediate fibers [18], which may be related to increases in the percentage and quantity of meat. Because ractopamine can promote changes in weight and nutrient use efficiency by maximizing muscle tissue gains, the weight and size of internal organs may also be modified. Additionally, amino acids not used by the organism must be catabolized by the body can cause liver and kidney overload, since these are the pathways for disposal of excess dietary nitrogen. It therefore appears that ractopamine promotes improved weight

gain and feed conversion for improved metabolic efficiency with lower demands for nitrogen elimination.

Add to this the fact that increases in temperature result in anatomical and physiological changes in animals, such as reduction in the weight of the gastrointestinal tract and viscera in an attempt to reduce the caloric increase in order to decrease endogenous heat [30, 34]. Thus, the beneficial results of ractopamine on carcass traits (Table 2) can be obtained both in animals maintained in conditions of thermal comfort and in animals kept in conditions of heat stress, since there is no interaction between the ractopamine levels and environmental temperature.

As was to be expected, the environmental temperature influences the carcass yield possibly by reducing gastrointestinal tract as aforesaid. In the same direction, both the ractopamine level used as the environment temperature affect the percentage of muscle tissue and reduces the backfat thickness in carcasses of pigs in the finishing phase

The effect of ractopamine on the percentage and amount of meat on the carcass of animals consuming diets with higher energy levels also has been demonstrated [3, 11]. Ractopamine results in a reduction in back-fat thickness and increases the percentage of meat, carcass yield and loin depth [4, 23, 46], significantly improving animal performance without affecting meat quality in terms of color, hardness, pH, and marbling [4, 47, 48].

One of the carcass parameters that have been more influenced by ractopamine is back-fat thickness. Has been observed that the inclusion of 20ppm of ractopamine in diets containing high levels of energy, between 2,548 and 2,668 kcal of net energy, caused a reduction in back-fat thickness [8]. Has been reported also linear decrease in back-fat thickness and linear increase of the depth of muscle and percentage of meat on the carcass due to the effects of ractopamina [12].

Table 2: Influence of Levels of Ractopamine Upon Carcass Quality

Variáveis	Ractopamine Levels (ppm)					CV (%)	Valor P		
	0	5	10	15	20		R ¹	T ²	R*T ³
Carcass, kg	77	78,1	79,2	79,9	77,1	4,47	0,473	0,079	0,72
Carcass yield, %	77,5	78,4	77,1	77	81,1	2,48	0,224	0,025	0,75
Lean meat, %	57,1	58,9	56,8	60,9	58,8	1,12	<,0001	<,0001	0,98
Backfat thickness, mm	13,2	13,1	11,4	13,7	8,7	6,92	0,026	0,096	0,71

¹R, effect of ractopamina level;

²T, effect of temperature environmental, and

³R*T, interaction of ractopamine versus temperature.

However, it has been found that the carcass traits have improved as a result of the use of ractopamine while not altering meat quality. When evaluating the inclusion of 10ppm of ractopamine in the diet of pigs was found that the values of initial and final pH of the meat, carcass temperature 45 minutes after slaughter, degree of marbling and tenderness of the meat were affected by inclusion of the additive [49]. The reduction in marbling may be indicative of increased diameter of muscle fibers associated with reduced lipogenesis and increased lipolysis of adipose tissue. Has been found also that increasing doses of ractopamine in the diet resulted in less red meat production, with less saturation and less marbling; however these changes do not compromise the sensory evaluation of meat and were not indicative of PSE (pallid, soft and exudative) [43].

It appears that the increase in muscle fibers did not alter the concentrations of calpain and this causes the meat quality to remain within the normal range due to the increase in efficiency of muscle growth without fat, resulting in less degradation after the death of myofibrillar protein [50].

With respect to weight and size of the organs, was found that animals under conditions of heat stress showed reduced weight of the liver, kidney, lung, spleen, heart and small intestine, and they also encountered a decrease in nutrient utilization efficiency by the animals subjected to heat stress [46]. In studies performed, animals fed diets with 0 or 20ppm of ractopamine showed greater utilization efficiency of amino acids in the diet and as a result, had lower absolute weights of the liver (1,322 vs. 1,160 g) and kidneys (290 vs. 255 g), and showed no effect on the weights of lungs, heart, spleen and small intestine when compared to animals that did not receive ractopamine in the diet [34].

Based on these facts, it appears that ractopamine affects the carcass characteristics of pigs at slaughter weighing more than 120.0 kg by decreasing back-fat thickness and increasing the proportional quantities of meat, but not altering the quality of meat; however ractopamine also affects the size of some organs such as liver and kidneys and in conditions of heat stress decreases the size of the gastrointestinal tract.

CURRENT PERSPECTIVES

The β -adrenergic have effectiveness in improving the efficiency of nutrient utilization and altered the body composition, mainly by reducing the fat content of

carcasses in livestock [4, 31, 32]. However, they have been lifted hypothesized to greater susceptibility to stress and higher incidences of lesions in animals treated with these compounds [44, 45], in addition to having fast desensitization of the β -adrenergic receptors [5]. The ractopamine has also been restricted in European countries since 1996, so the searches for similar products have increased in recent years.

Ractopamine hydrochloride has been marketed as a food additive. Because the most of the β -adrenergic receptors act over rate of growth and over body composition, mainly by reducing fat and increasing the efficiency of nutrient utilization. The carcass weight, percentage of fat and loin eye area also were improved [39]. Thus, given the finding of the effects of ractopamine hydrochloride, other products have been developed and tested to check if its effects are similar to the ractopamine such as astaxanthin (3,3'-dihydroxy- β , β -carotene-4, 4' dione) as studied [51]. This product acts on immunity [52] and quality of eggs [52]. It also acts improving the performance of sows before farrowing, during lactation, after weaning and over the meat quality of finishing pigs [53, 54].

TENDENCIES AND FUTURE DEVELOPMENTS

Diets for finishing pigs weighing more than 95.0kg which present adequate levels of amino acids and energy, and higher levels of available phosphorus can increase the efficiency of use of ractopamine.

Actions mediated by ractopamine may alter amino acid requirements, especially lysine content in diets with corresponding increases of other essential amino acids and metabolizable energy needs must be corrected. Therefore, the use of ractopamine is conditioned to the nutritional corrections of diets and studies are necessary to determine supplementation limits which do not become excessive and are excreted as environmental pollutants.

The reduced number of studies, with necessary nutritional corrections and animals weighing more than 90.0kg, relating ractopamine with high temperature environments leaves doubts as to the effects of the supplement in the diverse production environments. Thus, new studies are needed to evaluate performance, nutrient requirements, carcass traits and physiological changes due to the type of environment in which the animal is raised.

There is a need for more research relating to the effects of ractopamine with the welfare of pigs with at least 95.0 kg.

Ractopamine improves the carcass traits of pigs at slaughter weighing more than 120.0 kg, decreasing back-fat thickness and increasing the proportional quantities of meat, but not altering its quality. Ractopamine also affects the size of some organs such as the liver and kidneys and in conditions of heat stress decreases the size of the gastrointestinal tract.

ACKNOWLEDGEMENTS

The authors thanks to the INCT-CA (Instituto Nacional de Ciência e Tecnologia - Ciência Animal) for the financial support provided for the studies performed with ractopamine at the UFV (University Federal of Viçosa) and UFLA (University Federal of Lavras).

REFERENCES

- [1] Moreira I, Voorsluys T, Martins RM, Paiano D, Furlan AC, Silva MAA. Efeitos da restrição energética para suínos na fase final de terminação sobre o desempenho, característica de carcaça e poluição ambiental. *Acta Sci Anim Sci* 2007; 29: 179-85. <http://dx.doi.org/10.4025/actascianimsci.v29i2.223>
- [2] Corassa A, Lopes DC, Teixeira AO. Desempenho, características de carcaça e composição óssea de suínos alimentados com diferentes níveis de ractopamina e fitase. *R Bras Zootec* 2010; 39: 1740-47. <http://dx.doi.org/10.1590/S1516-35982010000800016>
- [3] Watanabe PH, Thomaz MC, Pascoal LAF, Ruiz US, Daniel E, Cristani J. Ractopamine in diets for finishing gilts. *R Bras Zootec* 2011; 40: 827-33. <http://dx.doi.org/10.1590/S1516-35982011000400017>
- [4] Marinho PC, Fontes DO, Silva FCO, Silva MA, Pereira FA, Arouca CLC. Efeito da ractopamina e de métodos de formulação de dietas sobre o desempenho e as características de carcaça de suínos machos castrados em terminação. *R Bras Zootec* 2007; 36: 1061-68.
- [5] Andretta I, Lovatto PA, Silva MK, Lehnen CR, Lanferdini E, Klein CC. Relação da ractopamina com componentes nutricionais e desempenho em suínos: um estudo meta-analítico. *Ciênc Rural* 2001; 41: 186-91. <http://dx.doi.org/10.1590/S0103-84782011000100030>
- [6] Apple JK, Maxwell CV, Brown DC, Friesen KG, Musser RE, Johnson ZB, Armstrong TA. Effects of dietary lysine and energy density on performance and carcass characteristics of finishing pigs fed ractopamine. *J Anim Sci* 2004; 82: 3277-87.
- [7] Webster MJ, Goodband RD, Tokach MD, Nelsen JL, Dritz SS, Unruh JA, et al. Interactive effects between ractopamina HCl and dietary lysine on finishing pig growth performance, carcass characteristics, pork quality and tissue accretion. *Prof Anim Sci* 2007; 23: 597-11.
- [8] Moura MS, Kiefer C, Silva CM, Santos AP, Fantini CC, Lucas LS. Energia líquida e ractopamina para leitoas em terminação sob altas temperaturas ambientais. *Ciênc Rural* 2011; 41: 1085-90. <http://dx.doi.org/10.1590/S0103-84782011000500025>
- [9] Schinckel AP, Wagner JR, Forrest JC, Einstein ME. Evaluation of alternative measures of pork carcass composition. *J Anim Sci* 2001; 79: 1093-19.
- [10] Lutz TR, Stahly TS. Effect of ractopamine on the optimum dietary phosphorus regimen for pigs. *Iowa State University Nutrition. Swine Res Rep ASL-R1796* 2002.
- [11] Corassa A, Lopes DC, Teixeira AO. Ractopamina e fitase em dietas para suínos na fase de terminação. *R Bras Zootec* 2009; 38: 2174-81. <http://dx.doi.org/10.1590/S1516-35982009001100015>
- [12] Sanches JF, Kiefer C, Moura MS, Silva CM, Luz MF, Carrijo AS. Níveis de ractopamina para suínos machos castrados em terminação e mantidos sob conforto térmico. *Ciênc Rural* 2010; 40: 403-408. <http://dx.doi.org/10.1590/S0103-84782009005000257>
- [13] Beermann DH. Beta-adrenergic receptor agonist modulation of skeletal muscle growth. *J Anim Sci* 2002; 80: 18-23.
- [14] Lehninger AL, Nelson DL, Cox MM. *Princípios de bioquímica*. 4th ed. Salvier: São Paulo 2007.
- [15] Ramos F, Silveira M. Agonistas adrenérgicos β 2 e produção animal: II - Relação estrutura-atividade e farmacocinética. *Rev Port Ciênc Vet* 2001; 96: 167-75.
- [16] Moody DE, Hancock DL, Anderson DB. Phenethanolamine repartitioning agents. In: *Farm Animal Metabolism and Nutrition*. D'Mello JPF, Ed. CAB International, New York 2000; pp. 65-95. <http://dx.doi.org/10.1079/9780851993782.0065>
- [17] Mills SE. Biological basis of the ractopamine response. *J Anim Sci* 2002; 80: 28-32.
- [18] See MT, Armstrong TA, Weldon WC. Effect of a ractopamine feeding program on growth performance and carcass composition in finishing pigs. *J Anim Sci* 2004; 82: 2474-80.
- [19] Schinckel AP, Li N, Richert BT, Preckel PV, Einstein ME. Development of a model to describe the compositional growth and dietary lysine requirements of pigs fed ractopamine. *J Anim Sci* 2003; 81: 1106-19.
- [20] Pérez A, Obispo NE, Claudio JP, Chicco CF. Efectos de la ractopamina y lisina sobre La deposición de grasa en cerdos seleccionados magros en La fase de engorde. *Zootec Trop* 2006; 24: 435-55.
- [21] Cantarelli VS, Fialho ET, Almeida EC, Zangeronimo MG, Amaral NO, Lima JAF. Características da carcaça e viabilidade econômica do uso de cloridrato de ractopamina para suínos em terminação com alimentação à vontade ou restrita. *Ciênc Rural* 2009; 39: 844-51. <http://dx.doi.org/10.1590/S0103-84782009000300032>
- [22] Armstrong TA, Ivers DJ, Wagner JR, Anderson DB, Weldon WC, Berg EP. The effect of dietary ractopamine concentration and duration of feeding on growth performance, carcass characteristics, and meat quality of finishing pigs. *J Anim Sci* 2004; 82: 3245-53.
- [23] Pereira FA, Fontes DO, Silva FCO, Ferreira WM, Lanna AMQ, Corrêa GSS, et al. Efeitos da ractopamina e de dois níveis de lisina digestível na dieta sobre o desempenho e características de carcaça de leitoas em terminação. *Arq Bras Med Vet Zootec* 2008; 60: 943-52. <http://dx.doi.org/10.1590/S0102-09352008000400025>
- [24] Lovatto PA, Lehnen CR, Andretta I, Carvalho AA, Hauschild L. Meta-análise em pesquisas científicas - enfoque em metodologias. *R Bras Zootec* 2007; 36: 285-94. <http://dx.doi.org/10.1590/S1516-35982007001000026>
- [25] Pena SM, Lopes DC, Rostagno HS, Silva FCO, Donzele JL. Relações metionina mais cistina digestível:lisina digestível em dietas suplementadas com ractopamina para suínos em terminação. *R Bras Zootec* 2008; 37: 1978-83. <http://dx.doi.org/10.1590/S1516-35982008001100012>
- [26] Almeida EC, Fialho ET, Rodrigues PB, Zangeronimo MG, Lima JAF, Fontes DO. Ractopamine and lysine levels on performance and carcass characteristics of finishing pigs. *R Bras Zootec* 2010; 39: 1961-68. <http://dx.doi.org/10.1590/S1516-35982010000900014>
- [27] Main RG, Dritz SS, Tokach MD, Goodband RD, Nelsen JL. Effects of feeding graded levels of ractopamine (paylean) on pig performance in a commercial finishing facility. *Kansas State University. Swine Day* 2001; 859: 74-76.

- [28] Brumm MC, Miller PS, Thaler RC. Response of barrows to space allocation and ractopamine. *J Anim Sci* 2004; 82: 3373-79.
- [29] Shelton JL, Southern LL, Lemieux FM, Bidner TD, Page TG. Effects of microbial phytase, low calcium and phosphorus, and removing the dietary trace mineral premix on carcass traits, pork quality, plasma metabolites, and tissue mineral content in growing-finishing pigs. *J Anim Sci* 2004; 82: 2630-39.
- [30] Manno MC, Oliveira RFM, Donzele JL, Oliveira WP, Vaz RGMV, Silva BAN, *et al.* Efeitos da temperatura ambiente sobre o desempenho de suínos dos 30 aos 60 kg. *R Bras Zootec* 2006; 35: 471-77.
<http://dx.doi.org/10.1590/S1516-35982006000200019>
- [31] Halas V, Verstegen MW, Gerrits. Efficiency of fat deposition from nonstarch polysaccharides, starch and unsaturated fat in pigs. *Br J Nutr* 2010; 103: 123-33.
<http://dx.doi.org/10.1017/S0007114509991449>
- [32] Latorre MA, Pomar C, Faucitano L, Gariépy C, Méthot S. The relationship within and between production performance and meat quality characteristics in pigs from three different genetic lines. *Livest Sci* 2008; 115: 258-67.
<http://dx.doi.org/10.1016/j.livsci.2007.08.013>
- [33] Rodrigues NEB, Zangeronimo MG, Fialho ET. Adaptações fisiológicas de suínos sob estresse térmico. *Revista Nutritime* 2010; 07: 1197-11.
- [34] Sanches JF, Kiefer C, Carrijo AS, Moura MS, Silva EA, Santos AP. Níveis de ractopamina para suínos machos castrados em terminação mantidos sob estresse por calor. *R Bras Zootec* 2010; 39: 1523-29.
<http://dx.doi.org/10.1590/S1516-35982010000700019>
- [35] Silva EA, Kiefer C, Moura MS, Bünzen S, Santos AP, Silva CM, *et al.* Duração da suplementação de ractopamina em dietas para leitoas em terminação mantidas sob alta temperatura ambiente. *Ciênc Rural* 2011; 41: 337-42.
<http://dx.doi.org/10.1590/S0103-84782011005000001>
- [36] Collin A Van, Milgen J, Dubois S, Noblet J. Effect of high temperature and feeding level on energy utilization in piglets. *J Anim Sci* 2001; 79: 1849-57.
- [37] Rezende WO, Donzele JL, Oliveira RFM, Abreu MLT, Ferreira AS, Silva FCO, *et al.* Níveis de energia metabolizável mantendo a relação lisina digestível:caloria em rações para suínos machos castrados em terminação. *R Bras Zootec* 2006; 35: 1101-106.
<http://dx.doi.org/10.1590/S1516-35982006000400022>
- [38] Ramos F, Silveira M. Agonistas adrenérgicos β_2 e produção animal: III - Efeitos zootécnicos e qualidade da carne. *Rev Port Ciênc Vet* 2002; 97: 51-62.
- [39] Trapp SA, Rice JP, Kelly DT, Bundy A, Schinckel AP, Richert BT. Evaluation of four ractopamine use programs on pig growth and carcass characteristics. West Lafayette: Purdue University, Swine Res Rep 2002; 62-71.
- [40] Marchant-Ford JN, Lay DC, Pajor EA, Lunstra BD, Rohrer GA, Ford JJ. The effects of ractopamine on the behavior and physiology of finishing pigs. *J Anim Sci* 2003; 81: 416-22.
- [41] Schaefer AL, Jones DM, Tong AKW, De Passile AMB, Rusher J, Merrill K. The effects of feeding the beta adrenergic agonistic ractopamine on the behavior of market weight pigs. *Canadian J Anim Sci* 1997; 72: 15-21.
<http://dx.doi.org/10.4141/cjas92-002>
- [42] Athayde NB. Desempenho, qualidade de carne e estresse de suínos suplementados com ractopamina. Dissertação de mestrado, Universidade Estadual Paulista, Botucatu, São Paulo, Brasil 2010.
- [43] Agostinic PS, Silva CA, Bridic AM, Abramic RAM, Pachecoc GD, Lozano AP, *et al.* Efeito da ractopamina na performance e na fisiologia do suíno. *Arch Zootec* 2011; 60: 659-70.
<http://dx.doi.org/10.4321/S0004-05922011000300054>
- [44] Poletto R, Rostagno MH, Richert BT, Marchant-Forde JN. Effects of a "step up" ractopamine feeding program, sex and social rank on growth performance, hoof lesions, and enterobacteriaceae shedding in finishing pigs. *J Anim Sci* 2009; 87: 304-11.
<http://dx.doi.org/10.2527/jas.2008-1188>
- [45] Poletto R, Cheng HW, Meisel RL, Garner JP, Richert BT, Marchant-Forde JN. Aggressiveness and brain amine concentration in dominant and subordinate finishing pigs fed the β_2 adrenoreceptor agonist ractopamina. *J Anim Sci* 2010; 88: 310-20.
<http://dx.doi.org/10.2527/jas.2009-1876>
- [46] Kiefer C, Sanches JF. Metanálise dos níveis de ractopamina em dietas para suínos em terminação. *R Bras Zootec* 2009; 38: 1037-44.
<http://dx.doi.org/10.1590/S1516-35982009000600010>
- [47] Herr CT, Yake W, Robson C, Kendall DC, Schinckel AP, Richert BT. Effect of nutritional level while feeding paylean to late-finishing swine. Purdue University; Swine Day 2000; 89-95.
- [48] Marinho PC, Fontes DO, Silva FCO, Silva MA, Pereira FA, Arouca CLC. Efeito dos níveis de lisina digestível e da ractopamina sobre o desempenho e as características de carcaça de suínos machos castrados em terminação. *R Bras Zootec* 2007; 36: 1791-98.
<http://dx.doi.org/10.1590/S1516-35982007000800012>
- [49] Bridi AM, Oliveira AR, Fonseca NAN, Shimokomaki M, Coutinho LL, Silva CA. Efeito do genótipo halotano, da ractopamina e do sexo do animal na qualidade da carne suína. *R Bras Zootec* 2006; 35: 2027-33.
<http://dx.doi.org/10.1590/S1516-35982006000700021>
- [50] Lonergan SM, Huff-Lonergan E, Rowe LJ, Kuhlers DL, Jungst SB. Selection for lean growth efficiency in duroc pigs influences pork quality. *J Anim Sci* 2001; 79: 2075-85.
- [51] Johnson E, An G. Astaxanthin from microbial sources. *Crit Rev in Biotechnol* 1991; 11: 297-26.
<http://dx.doi.org/10.3109/07388559109040622>
- [52] Chew BP, Park JS. Carotenoid Action on the Immune Response. *J Nutr* 2004; 134: 257S-261S.
- [53] Yang YX, Kim YJ, Jin Z, Lohakare JD, Kim CH, Ohh SH, *et al.* Effects of dietary supplementation of astaxanthin on production performance egg quality in layers and meat quality in finishing pigs. *Asian-Aust. J Anim Sci* 2006; 19: 1019-25.
- [54] Inbarr J, Campbell R, Luxford B, Harrison D, Lignell A. Improving sow and litter performance by feeding astaxanthin-rich algae meal. Proceedings of the 7th International Symposium on Digestive Physiology in Pigs 1997. Saint Malo, France. EAAP 1997; 88: 479-482.

Received on 12-01-2013

Accepted on 27-03-2013

Published on 08-04-2013

<http://dx.doi.org/10.6000/1927-5129.2013.09.36>© 2013 Ferreira *et al.*; Licensee Lifescience Global.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.