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The impact of growth promoters on muscle growth and the potential consequences for meat quality

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ABSTRACT

To meet the demands of increased global meat consumption, animal production systems will have to become more efficient, or at least maintain the current efficiency utilizing feed ingredients that are not also used for human consumption. Use of growth promoters is a potential option for increasing production animal feed efficiency and increased muscle growth. The objective of this manuscript is to describe the mechanisms by which the growth promoters, beta-adrenergic agonists and growth hormone, mediate their effects, with specific consideration of the aspects which have implications for meat quality.

1. Introduction

The predicted increase in world population to 9 billion by 2050 is expected to be associated with an increase in the urban population, with an estimated 70% being in an urban environment compared to 49% today and, hopefully, the inevitable increase in incomes (FAO, 2009). To meet this demand it is estimated that the food production will have to increase, particularly for commodities associated with higher incomes, such as meat, with the predicted demand more than doubling by 2050 (FAO, 2009).

To date, significant advances in animal genetics and animal nutrition have been made to meet the increasing demand. To achieve the maximum growth potential, high quality feed ingredients are required. Feed ingredients account for a large proportion of the overall costs of animal production, particularly in non-ruminant species (Patience, Rossoni-Serao, & Gutierrez, 2015). Continuing to rely on the same ingredients, in competition with human nutrition and biofuels, mean prices will inevitably increase. Therefore the cost of meat and animal products will also increase. It has been estimated that for many agricultural commodities the rate of production has already reached a peak (Seppelt, Manceur, Liu, Fenichel, & Klotz, 2014). Hence, if we are to continue to meet the demand for animal products, we cannot simply feed more animals the same feed ingredients, as that would require more crops, land and water (Foresight, 2011; Godfray et al., 2010). Therefore the aim of current research is to improve the efficiency with which animals utilize their feeds, giving more product for the same amount of feed or the same amount of product for less feed.

Through selective breeding and improved diet formulations over the last 20–30 years, feed efficiency of pigs (Patience et al., 2015) and chickens (Siegel, 2014) has improved, with Feed Conversion Ratio (FCR) values of 2.0 or less currently achievable (i.e. >50% efficiency). The UN suggests productivity is likely to be enhanced in the future through better animal disease control, improved irrigation and water management practises, and better fertilizers (FAO, 2009). In terms of animal production the increase in productivity could also be increased through the continued utilization of genetic selection through breeding programmes. Also it is probably inevitable that molecular biology technologies will be accepted and GMO organisms will be utilized for animal production. However throughout the world there is an increasing utilization of growth promoters. A goal of all these technologies is to increase the efficiency of feed utilization that ideally results in an increase in lean carcass weight. A predominant group of growth promoters are those which are based on endocrine factors such as anabolic steroids, growth hormone (GH, also called somatotropin, ST) and beta-adrenergic agonists (BA). These agents have metabolic modifying characteristics that result in enhanced growth. In addition there are a variety of other types of growth promoters, such as antibiotics, whose predominant affect is thought to be the increased efficiency of utilization of nutrients from the gut. Although the use of growth promoting agents is banned in the European Union (EU), they are legally used in many other countries.

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Increases in lean tissue deposition (increased muscle mass), decreases in fat deposition, along with repartitioning nutrients away from fat to muscle growth, are some of the predominant objectives of animal production systems focused on generating meat. Therefore these are key features of animal growth that growth promoters are designed to influence. The actions of hormonal based growth promoters' are through mechanisms that influence processes at a cellular level. In addition to affecting protein turnover to increase protein accretion, they also have effects on energy metabolism. This manuscript will examine the effects of hormonal based growth promoters on carcass parameters that influence meat quality, particularly growth hormone (GH) and beta-adrenergic agonists (BA), and will predominantly focus on their effects in pigs.

2. Growth hormone

Growth hormone is a peptide hormone produced by the anterior pituitary and is involved in the processes of development and growth that includes skeletal muscle, bone and adipose tissue (Beermann, 1994). Increased plasma GH has the effect of redirecting nutrients away from adipose tissue and toward muscle and bone (Etherton & Bauman, 1998). The effect of GH is to stimulate the production of insulin like growth factor (IGF-1) from the liver. These observations led to the hypothesis that GH effects, particularly on growth, were mediated by IGF-1 originating from the liver (Daughaday, 2000). However GH can stimulate IGF-1 expression in other tissues, particularly bone but also skeletal muscle (Brameld et al., 1996; Velloso, 2008: Wang, Bikle, & Chang, 2013). In the circulation IGF-1 is associated with insulin like growth factor binding proteins (IGFBP) which prolong its half-life (Boisclair, Rhoads, Ueki, Wang, & Ooi, 2001). The effect of IGF-1 can be mediated through dimers of the IGF-1 receptor as well as IGF-1 receptor/insulin receptor hybrids (Denley, Cosgrove, Booker, Wallace, & Forbes, 2005) and subsequently activates multiple signalling pathways. In muscle the predominant pathways are the mitogen-activated protein kinase kinase/ extracellular signal-regulated kinase (MEK/ERK pathway, which tends to be associated with proliferative growth, whilst the protein kinase B -mechanistic target of rapamycin - ribosomal protein S6 kinase (Akt–mTOR–S6K) pathway is predominantly responsible for protein synthesis but also affects protein degradation (Clemmons, 2009).

Growth hormone is approved for use in 14 countries, including Australia, for administration to pigs to improve growth characteristics (Dunshea, Cox, Borg, Sillence, & Harris, 2002). As the GH is a peptide it has to be administered by regular injection. Its action on pig growth has been well characterized, reducing feed intake whilst simultaneously increasing lean and reducing fat deposition (Etherton et al., 1987). Unsurprisingly, due to the signalling pathway activated by GH-IGF-1 axis, increased protein accretion in GH treated pigs is stimulated by protein synthesis rather than a decrease in protein degradation. However there are inconsistent reports in the literature with some reporting similar increases in protein synthesis and breakdown but overall net increased nitrogen balance (Tomas et al., 1992), whilst others have reported that protein synthesis is increased but protein degradation appears not to be affected (Bush et al., 2003) and some have described even a decrease in degradation (Vann et al., 2000). The effect of exogenous GH on adipose tissue is to reduce fat synthesis which results in reductions in back fat (Krick et al., 1992). Dunshea, D'Souza, Pethic, Harper, and Warner (2005) carried out a comprehensive review on the effects of GH on pig meat quality. Using a meta-analysis approach on published data, they concluded that GH decreased intramuscular fat by 12% and increased shear force by 9%. The effects on shear force are unlikely to be due to a large decrease in the proteolytic activity. Therefore the increased shear force is likely to be due to changes in temperature transfer to the meat, either during chilling the carcass, thereby affecting rigour development or effects of heat transfer during cooking which influences denaturing of proteins. Overall Dunshea et al. (2005) concluded that GH causes a small increase in shear force and the sensory perception of meat from treated pigs is tough, but it was unlikely that that this could be detected by consumers.

3. Beta-adrenergic agonists

The BAs are analogues of the endogenous catecholamines, adrenaline and noradrenaline. When administered to livestock species they have positive effects on growth and nutrient repartitioning. Beta-2 adrenergic receptor specific agonists, such as clenbuterol and cimaterol, have the greatest growth effect; however ractopamine, which binds to both beta-1 and -2 adrenergic receptors (Mills, Kissel, Bidwell, & Smith, 2003), also has similar growth effects. The BA generally have positive effects on weight gain, FCR, and act as strong repartitioning agents, increasing muscle growth whilst decreasing adipose tissue deposition (Meersman, 1998).

The BAs mediate their growth effects through the BA receptor. The subtypes of beta adrenergic receptors (BAR) vary depending on the tissue. For example, in pigs skeletal muscle has more BAR2 than BAR1 whilst in adipose tissue it is the reverse (Liang & Mills, 2002). BAR3 are thought to be present on porcine adipocytes (McNeel & Mersmann, 1995). The BAR activates the adenylate cyclase pathway which subsequently produces cyclic adenosine monophosphate (cAMP), which then activates protein kinase A. This kinase can alter enzyme activity through phosphorylation. For example the phosphorylation dependent cascade results in phosphorylase being activated and glycogen being degraded to glucose-1-phosphate. In addition, protein kinase A can activate the transcription factor, cAMP response element binding protein (CREB), which then regulates the transcription of genes that have a functional cAMP responsive element within their regulatory regions (Altarejos & Montminy, 2011). Therefore these agents have an immediate effect on enzyme activity, but can also alter transcription of a number of genes.

The first BA to be licenced for use as a feed additive was ractopamine for use in pigs in 1999. A significant advantage of these agents when compared to GH is that they can be administered in feed. The predominant effect of BA is to increase lean deposition whilst also decreasing fat deposition (Meersman, 1998). The BAs have strong effects on muscle hypertrophy and appear to be differentially effective across farm species, with ruminant species (cattle and sheep) responding the strongest, being particularly effective in older animals (Meersman, 1998). The early studies on the effects of BA in livestock indicated that these agents had a strong effect of decreasing protein degradation without increasing protein synthesis (Bohorov, Buttery, Correia, & Soar, 1987). However subsequent studies in pigs treated with ractopamine have indicated that protein synthesis, particularly of myofibrillar proteins, is stimulated (Adeola, Ball, & Young, 1992). The effects on fat deposition are not as clear as for GH, particularly in pigs, however it appears that ractopamine reduces backfat thickness in pigs, but this is not as dramatic as the effect of BA in ruminant species (Dunshea et al., 2005). After reviewing a large number of studies, Dunshea et al. (2005) concluded that the use of BA in ruminants increased the shear force, with cimaterol increasing shear force by 60%. Using a meta-analysis approach on published data they also described how, in pigs, the BAs ractopamine and salbuterol had no effect on IMF, whilst cimaterol caused a decrease. All these BA had the effect of increasing shear force in pigs, but again cimaterol had the greatest negative effect, but the effects were not as great as in ruminants. Unlike GH, the effect of BA on tenderness appears to be mediated through their strong inhibitory effects on protein degradation (see below), rather than effects on IMF.

4. Fibre type and meat quality

Skeletal muscle is made up of muscle fibres which have differing contractile and metabolic characteristics. Muscle fibres can be histochemically classified according to their actomyosin ATPase activity into three types, types I, IIA and IB, which have a contractile and