The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

Brameld, John M. and Parr, Tim (2016) Improving efficiency in meat production. Proceedings of the Nutrition Society . ISSN 0029-6651

Improving efficiency in meat production

John M. Brameld and Tim Parr

School of Biosciences, University of Nottingham, Loughborough, Leics. LE12 5RD, UK

Abstract

Selective breeding and improved nutritional management over the last 20-30 years has resulted in dramatic improvements in growth efficiency for pigs and poultry, particularly lean tissue growth. However, this has been achieved using high quality feed ingredients, such as wheat and soya, that are also used for human consumption and more recently biofuels production. Ruminants on the other hand are less efficient, but are normally fed poorer quality ingredients that cannot be digested by humans, such as grass or silage. The challenges therefore are to (i) maintain the current efficiency of growth of pigs and poultry, but using more ingredients not needed to feed the increasing human population or for the production of biofuels; (ii) improve the efficiency of growth in ruminants; and (iii) at the same time produce animal products (meat, milk and eggs) of equal or improved quality. This review will describe the use of a) enzyme additives for animal feeds, to improve feed digestibility; b) known growth promoting agents, such as growth hormone, beta-agonists and anabolic steroids, currently banned in the EU but used in other parts of the world; and c) recent transcriptomic studies into molecular mechanisms for improved growth efficiency via low Residual Feed Intake (RFI). In doing so, the use of Genetic Manipulation in animals will also be discussed.

Feed efficiency: Meat: Enzymes: Growth promoters

Introduction

It is widely predicted that the world population will increase to 9 billion by 2050 [1-2]. At the same time, economic improvements in developing countries around the world are predicted to result in an increased demand for meat, milk and other animal products, as those societies become more “westernised”. Even though there are calls for people in developed countries to reduce meat consumption for health reasons, particularly processed red meat, the demand for meat is predicted to continue to increase at a similar rate to that seen in the previous 10+ years. Over the last 50 years, tremendous advances in animal genetics and animal nutrition have been made to meet the increasing demand, particularly in pigs and poultry, but this has mainly been achieved using high quality feed ingredients such as wheat, maize and soya. Over recent years these ingredients have become increasingly more expensive, due to a combination of increased demand from the biofuels industry, as well as for animal and human nutrition, along with shortages due to crop failures in some parts of the world. It has been estimated that for many agricultural commodities the rate of production has already reached a peak [3]. 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 [1-2].

Feed ingredients account for a large proportion of the overall costs of animal production, particularly in non-ruminant species [4]. Continuing to rely on the same ingredients, in competition with human nutrition and biofuels, mean prices will increase and therefore the cost of meat and animal products will also increase. Therefore the aim of current research is to improve the efficiency with which animals utilise their feeds, giving more product for the same amount of feed or the same amount of product for less feed. This is referred to as Feed Efficiency (FE), which is simply calculated as the change in body weight divided by the change in feed intake (kg gain/ kg feed). Hence increased efficiency would be greater gain per unit feed. Another term used is Feed Conversion Ratio (FCR), which is the kg feed per kg gain, with improved efficiency associated with a lower FCR value (less feed per unit gain). More recently animal scientists refer to Residual Feed Intake (RFI), which compares the feed intake for each individual animal to the average for the herd/ group at the same rate of growth [4]. Hence an animal with a low RFI (often a negative value) would be eating less for the same growth rate and therefore be more efficient than an animal with a high RFI (a positive value), which would be eating more.

There is no doubt that selective breeding and improved diet formulations over the last 20-30 years have improved the feed efficiency of pigs [4] and chickens [5], with FCR values of 2.0 or less currently achievable (i.e. >50% efficiency). Indeed it is predicted that FCR values of 1.5 and less will be seen relatively soon for both pigs and chickens (note that the lowest value theoretically possible would be 1.0, meaning 100% efficiency). In contrast, ruminants are a lot less efficient [6], with FCR values of 5.0 or more being normal (i.e. <20% efficiency). However we must remember that ruminants can utilise ingredients not used for human consumption (e.g. grass and silage) and are therefore not competing with humans, non-ruminants and biofuels for the high quality ingredients. Feed efficiency can be improved in ruminants by feeding higher quality ingredients as concentrates [7], but that is not the solution for the future. What we need is to maintain or improve the efficiency of livestock, while at the same time maintaining or improving the quality of the animal products, but using alternative (human inedible) feed ingredients as much as possible. In that way we will be converting human inedible ingredients into high quality, human edible foods. This review will highlight a few ways in which this is being achieved or might be achieved in the future.

Use of enzymes as feed additives

A number of enzymes are already used commercially as feed additives, particularly in non-ruminant (pig and poultry) feeds, to increase the digestion and subsequent absorption of nutrients [(8-10)]. They are mainly used to improve the digestion of feed components that the animals cannot normally digest or are only able to digest fairly poorly, such as complex carbohydrates and phytate. By increasing the digestibility of the feed, more nutrients enter the body and less pass through in the faeces, resulting in increased growth for the same level of feed intake, hence improving feed efficiency.

A number of enzyme feed additives are commercially available to improve the digestibility of cereal carbohydrates, particularly targeting xylans and arabinoxylans present in the cell walls [(9)]. By digesting these important structural carbohydrates in the cell wall, that then allows the animals' own carbohydrate-digesting enzymes (e.g. α-amylase) better access to the main starch stores within the plant cells. Secondly, the digestion reduces the viscosity problems associated with arabinoxylans and β-glucans [(9)]. A number of studies have shown improved feed efficiency/ FCR of pigs and chickens when these enzymes are added to the feed. For example, Xylanase supplementation of feed was shown to improve FCR (1.41 vs 1.56 in controls) in broiler chickens by increasing weight gain, but not affecting feed intake [(11)]. As well as increasing the digestibility of the carbohydrate component of the feed and reducing the viscosity, there are suggestions that these carbohydrate-degrading enzymes might have prebiotic actions on the gut microflora via the oligosaccharides they produce [(9)]. This could be another potential mechanism for their effects on feed efficiency. The absorption of nutrients across the gut is also known to affect production of gut peptides, which can subsequently alter gut motility and feed intake. Indeed Xylanase supplementation of feed has been shown to increase plasma PYY levels in broiler chickens [(12)] and we have recent data showing effects of Xylanase supplementation on plasma peptide YY, gastric inhibitory polypeptide and glucagon-like peptide-1 concentrations in young pigs [(13)]. Hence the regulation of gut peptides and their subsequent effects on gut motility, feed intake and/or nutrient utilisation might be additional, alternative mechanisms for the effects of these carbohydrate-degrading enzymes on feed efficiency.

Phytase is another enzyme used commercially in non-ruminant (pig and poultry) feeds [10]. Phytase digests Phytate (also called Phytic acid or inositol hexakisphosphate, IP6), the main storage form for Phosphorus (P) in plants. Phytate (IP6) is inositol with 6 phosphate groups attached and phytase is able to cleave individual phosphate groups, thereby releasing them for absorption and use by the animal. Phytase supplementation results in greater absorption of P and calcium (Ca) from the feed in broiler chickens and pigs [14], resulting in increased growth and reduced FCR. However, the increased growth may not simply be due to increased absorption of these important micronutrients. Chicken studies [15] have shown that high levels of Phytate in the diet inhibit pepsin and trypsin activities and therefore inhibit protein digestion and amino acid absorption, resulting in increased FCR. Inclusion of Phytase as well as high Phytate in the diet reduced the inhibitory effect on proteolysis, resulting in improved (reduced) FCR [15].

Both of these feed additive enzymes have positive effects on feed efficiency in pigs and chickens fed cereal-based diets. They do so by different mechanisms, meaning their benefits are likely to be additive, but importantly they may allow the use of poorer quality (i.e. human inedible) feed ingredients, an important consideration for future sustainability and food security. These and other enzymes are also being investigated for use in ruminants [16].

Use of growth promoters/ metabolic modifiers/ anabolic agents

There are 3 main classes of growth promoters [17] – beta-adrenergic agonists (BA), anabolic steroids and growth hormone (GH, also called somatotropin, ST). They all improve feed efficiency in livestock to some extent and this is associated with increased lean mass (particularly skeletal muscle) and reduced fat mass [17]. Indeed they have all been in the news at different times in relation to their illegal use as performance enhancing drugs in sportsmen and women. Their effects on muscle and fat mass were first discovered in the 1950s (anabolic steroids) or 1980s (BA and GH) and a number of commercial products are currently licenced for livestock production around the world [17], although they are all banned in the EU. For example, Ractopamine and Zilpaterol (both BA) are licenced for use in pigs and/or cattle in North and South America, South Africa, India and Australia, but not China. Similarly, the anabolic steroid mix of Trenbolone Acetate and Oestradiol (TBA & E2) is licenced for use in beef cattle in North and South America, South Africa, India, Australia and China and GH (either bovine or porcine ST) is licenced for use in dairy cattle or pigs in the same areas. We were unable to find information for other parts of the world (e.g. Northern Africa and other parts of Asia), so to our knowledge only the EU has a total ban on the use of these agents in livestock production. This is despite much of the early research work being carried out in the EU, especially the UK, and the original scientific reports suggesting their use was safe [18], as long as appropriate guidelines were followed (e.g. a withdrawal period prior to slaughter).

At Nottingham, we have been comparing the molecular modes of action of BA and GH in both sheep[19-21] and pigs[22-24] combining transcriptomic and metabolomics technologies in a systems biology approach to identify novel mechanisms to achieve the same effects. Ultimately the aim is to identify novel target genes/ proteins to develop more acceptable drugs or for targeted breeding or nutritional manipulations. We have made good progress and have identified upregulation of the serine biosynthesis pathway [19; 21; 23] and a number of other novel changes in response to BA and/or GH treatments. We are currently performing proof-of-principle studies to determine whether the novel genes we have identified really do regulate growth, body composition and/or feed efficiency. If successful, the next stage will be to use this information to develop breeding strategies, new dietary regimens or drugs that result in improved feed efficiency in livestock.

For proof-of-principle studies we often utilise transgenic animals (mainly mice) where the gene of interest is either over-expressed or knocked out/ down (i.e. genetic manipulation or GM), often in a tissue-specific manner. This is done to investigate whether manipulation of the specific gene results in the predicted changes in tissue growth and/or metabolism, as well as changes in feed efficiency or whole body energy expenditure. Such studies cannot be performed in cultured cells, so must be done in animals. Although technically challenging, GM can now be achieved in livestock [25], so that it will theoretically be possible to produce herds of transgenic livestock. Indeed the Chinese government is funding work using GM aimed at developing new breeds of livestock for agricultural use in the future, including research into their safety [26]. One of the main advantages of GM over conventional animal breeding is that GM speeds up the process and is more gene specific; whereas conventional breeding, while very successful over the last 50 years, can result in unwanted side effects, both on animal welfare but also product quality. The halothane pig [27] and Callipyge sheep [28] are prime examples of this. Both have increased growth rates, particularly muscle, but one (halothane) results in highly stressed pigs and both result in poorer meat quality.

Molecular studies of low Residual Feed Intake (RFI) animals

The concept of low and high RFI has progressed rapidly over recent years [(29-30)]. Studies are being carried out around the world aimed at identifying specific genes (or markers) for improved feed efficiency in virtually all livestock species (cattle, pigs, sheep, poultry). The genetic approach has been to identify markers (Quantitative Trait Loci, QTL, or Single Nucleotide Polymorphisms, SNPs) of low RFI for subsequent use in selective breeding programmes. For example, a Chinese group [(31)] recently identified a SNP in a microRNA (miR-1596) gene in chickens that resulted in reduced expression of miR-1596 in livers and was associated with low RFI. Interestingly, they suggested there were more than 70 target genes for miR-1596 [(31)], which were mainly involved in energy metabolism, apoptosis and immune responses, with some being important proteins for assembling mitochondria.

We collaborated with another Chinese group [(32)], to investigate differential gene expression in skeletal muscle from pigs with low vs high RFI using a deep sequencing (RNAseq and miRNAseq) approach. A number of mRNA (IGF2, FABP3 and PGC1a) and miRNA (miR1, miR30, miR10b, miR145) were found to be differentially expressed, but importantly the majority of mitochondrial genes were down-regulated. The data suggested that low RFI was linked with changes in expression of mRNA and miRNA associated with increased muscle growth and reduced mitochondrial activity in skeletal muscle [(32)].

Effects on mRNA or miRNA associated with mitochondria appear to be a recurring theme in the low RFI studies [(33-34)] and this agrees with some of our growth promoter studies, where we also see down-regulation of a number of genes associated with mitochondria, including both Tricarboxylic Acid cycle and oxidative phosphorylation genes (unpublished data).

Once again the genes being identified in these various RFI studies could be potential targets for novel drugs, dietary regimens or GM in animals, as well as being used for conventional breeding strategies to improve feed efficiency in livestock.

Conclusions

There are tools already available to improve feed efficiency in meat production, including the use of enzyme feed additives and growth promoters. Recent molecular studies are starting to identify other mechanisms that might be utilised in the future, including manipulation of gut microflora or gut peptides and targeting of gene expression in skeletal muscle or other tissues using drugs or GM technologies. Whether the use of drugs or GM technologies will be acceptable to the EU general public in the future remains to be seen, but we cannot simply wait until food and meat availability becomes limited (or very expensive) before starting research on these more controversial topics. At present, food and meat are readily accessible and reasonably affordable throughout most of the EU, so the current ban on the use of growth promoters does not really affect the consumer. However this might change if feed ingredients continue to increase in price and there are issues with crop failures around the world limiting their availability for animal feeds. The EU might then have to reconsider the ban or accept that meat and animal products will become more expensive and less accessible, as well as potentially limiting the countries we import meat from. We should emphasise that safety and quality of the products will always be a primary concern and must not be ignored in the drive to improve feed efficiency for meat production. Indeed we would suggest that research into the safety aspects must be carried out alongside the research into the manipulation of feed efficiency, as is currently happening in China. Finally, we suggest that greater emphasis is needed on the use of "poorer quality" ingredients in animal feeds in future, to reduce the competition with human nutrition and biofuels for the high quality ingredients, such as wheat, maize and soya.

Acknowledgements

We would like to acknowledge the numerous PhD students and collaborators (both academic and industrial) that have contributed to the work included in this review, of which there are too many to name.

Financial Support

The work included has been funded by the Biotechnology and Biological Sciences Research Council (BBSRC), Zoetis (formerly Pfizer Animal Health) and AB Vista.

Conflicts of Interest

The studies we have done on feed enzymes have been funded by AB Vista and the recent growth promoter studies are funded by Zoetis/ Pfizer Animal Health.

Authorship

Both authors contributed equally to the planning and writing of this manuscript.

References

1. Foresight. (2011) The Future of Food and Farming: Challenges and choices for global sustainability. Final Project Report. The Government Office for Science, London. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/288329/11-546-future-of-food-and-farming-report.pdf
2. Godfray, HCJ, Beddington, JR, Crute, IR, et al. (2010) Food security: The challenge of feeding 9 billion people. *Science* **327**, 812-818.
3. Seppelt, R, Manceur, AM, Liu, J, et al. (2014). Synchronized peak-rate years of global resources use. *Ecology and Society* **19**(4), 50. DOI 10.5751/ES-07039-190450
4. Patience, JF, Rossoni-Serao, MC & Gutierrez, NA (2015) A review of feed efficiency in swine: biology and application. *Journal of Animal Science and Biotechnology* **6,** 33. DOI 10.1186/s40104-015-0031-2.
5. Siegel, PB (2014) Evolution of the modern broiler and feed efficiency. *Annual Review of Animal Biosciences* **2,** 375-385.
6. Berry, DP & Crowley, JJ (2013) Cell Biology Symposium: Genetics of feed efficiency in dairy and beef cattle. *J. Anim. Sci.* **91,** 1594–1613. doi:10.2527/jas2012-5862.
7. Martin, C, Morgavi, DP & Doreau, M (2010) Methane mitigation in ruminants: from microbe to the farm scale. *Animal* **4**(3), 351-365. doi: 10.1017/S1751731109990620.
8. Bedford MR & Schulze H (1998) Exogenous enzymes for pigs and poultry. *Nutrition Research Reviews* **11**, 91-114.
9. Masey O'Neill, HV, Smith, JA & Bedford, MR (2014a) Multicarbohydrase enzymes for non-ruminants. *Asian-Australasian Journal of Animal Sciences* **27**(2), 290-301.

10. Humer, E, Schwarz, C & Schedle, K (2015) Phytate in pig and poultry nutrition. *Journal of Animal Physiology and Animal Nutrition* **99,** 605-625.
11. Amerah, AM, Mathis, G & Hofacre, CL (2012) Effect of xylanase and a blend of essential oils on performance and Salmonella colonization of broiler chickens challenged with Salmonella Heidelberg. *Poultry Science* **91**, 943-947.
12. Singh, A, Masey O'Neill, HV, Ghosh, TK, et al. (2012) Effects of xylanase supplementation on performance, total volatile fatty acids and selected bacterial population in caeca, metabolic indices and peptide YY concentrations in serum of broiler chickens fed energy restricted maize-soybean based diets. *Animal Feed Science and Technology* **177**, 194-203
13. May, K, O'Sullivan, SE, Brameld, JM, et al. (2015) Xylanase supplementation in weaned piglets and its effect on gut hormone production. *J. Anim. Sci.* **93** Suppl. s3, 201.
14. Simons, PCM, Versteegh, HAJ, Jongbloed, AW, et al. (1990) Improvement of phosphorus availability by microbial phytase in broilers and pigs. *Br. J. Nutr* **64**, 525-540.
15. Liu, N, Ru, YJ, Li, FD, Wang, JP & Lei, XQ (2009) Effect of dietary phytate and phytase on proteolytic digestion and growth regulation of broilers. *Archives of Animal Nutrition* **63**(4), 292-303.
16. Masey O'Neill, HV, Bedford, MR & Walker, N (2015) Recent developments in feed enzyme technology. In *Recent Advances in Animal Nutrition 2014,* pp. 97-106 [PC Garnsworthy and J Wiseman, editors]. Context Products Ltd, Packington, Leics., UK.
17. Sillence, MN (2004) Technologies for the control of fat and lean deposition in livestock. *The Veterinary Journal* **167,** 242-257.
18. Lamming, GE, Ballarini, G, Baulieu, EE, et al. (1987) Scientific report on anabolic agents in animal production. Scientific working group on anabolic agents. *The Veterinary Record* **121**(17), 389-392. doi:10.1136/vr.121.17.389.
19. Al-Doski S, Parr T, Hemmings, K, et al. (2015). The effects of growth promoting agents on ovine metabolism and growth (Abstract 112). *J. Anim. Sci.* **93**(Suppl. s3)/ *J. Dairy Sci.* **98**(Suppl. 2), 224.
20. Hemmings, KM, Parr, T, Daniel, ZCTR, et al. (2015). Differential effects of short term β agonist and Growth Hormone treatments on expression of Myosin Heavy Chain IIB and

associated metabolic genes in sheep muscle. *Animal* **9**(2), 285-294. Doi: 10.1017/S175173111400233X.

21. Parr, T, Al-Doski, S, Hemmings, K, et al. (2015). Increased expression of serine biosynthetic pathway genes is associated with skeletal muscle hypertrophy in sheep. *Proc Nutr Soc* **74** (OCE2), E183.
22. Brameld, JM, Atkinson, JL, Saunders, JC, et al. (1996). Effects of Growth Hormone administration and dietary protein intake on Insulin-like growth factor-I and Growth Hormone Receptor mRNA expression in porcine liver, skeletal muscle and adipose tissue. *J. Anim. Sci.* **74,** 1832-1841.
23. Brameld J, Ryan K, Williams H, et al. (2015). Transcriptomic and metabolomic assessment of growth promoter effects on porcine muscle growth (Abstract 109). *J. Anim. Sci.* **93**(Suppl. s3)/ *J. Dairy Sci.* **98**(Suppl. 2), 223.
24. Sensky, PL, Jewell, KK, Ryan, KJP, et al. (2006) Effect of anabolic agents on calpastatin promoters in porcine skeletal muscle and their responsiveness to cyclic adenosine monophosphate- and calcium-related stimuli. *J. Anim. Sci.* **84**(11), 2973-2982.
25. Niemann, H, Kuhla, B & Flachowsky, G (2011) Perspectives for feed-efficient animal production. *J. Anim. Sci.* **89**(12), 4344–4363. doi: 10.2527/jas.2011-4235.
26. USDA FAS GAIN Report Number CH11002 (2011) China - Peoples Republic of Biotechnology – GE Plants and Animals. http://gain.fas.usda.gov/Recent GAIN Publications/Biotechnology – GE Plants and Animals_Beijing_China – Peoples Republic of_3-15-2011.pdf
27. Rosenvold, K & Andersen, HJ (2003) Factors of significance for pork quality – a review. *Meat Science* **64,** 219-237.
28. Tellam, RL, Cockett, NE, Vuocolo, T et al. (2012) Genes contributing to genetic variation of muscling in sheep. *Frontiers in Genetics* **3,** 164. doi: 10.3389/fgene.2012.00164.
29. Herd, RM, Oddy, VH & Richardson, EC (2004) Biological basis for variation in residual feed intake in beef cattle. 1. Review of potential mechanisms. *Australian Journal of Experimental Agriculture* **44,** 423-430.
30. Sartin, JL (2013) Cell Biology Symposium: Molecular basis for feed efficiency. *J. Anim. Sci.* **91**, 1580–1581.

31. Luo, C, Sun, L, Ma, J, et al. (2015) Association of single nucleotide polymorphisms in the microRNA miR-1596 locus with residual feed intake in chickens. *Animal Genetics* **46**(3), 265-271.

32. Jing, L, Hou, Y, Wu, H, et al. (2015) Transcriptome analysis of mRNA and miRNA in skeletal muscle indicates an important network for differential Residual Feed Intake in pigs. *Scientific Reports* **5,** 11953.

33. Bottje, W & Kong, B-W (2013). Cell Biology Symposium: Feed efficiency: Mitochondrial function to global gene expression. *J. Anim. Sci.* **91,** 1582–1593

34. Grubbs, JK, Huff-Lonergan, E, Gabler NK, et al. (2014). Liver and skeletal muscle mitochondria proteomes are altered in pigs divergently selected for residual feed intake. *J. Anim. Sci.* **92,** 1995-2007.