INVITED REVIEW

THE ROLE FOR HORMONAL GROWTH PROMOTANTS AND OTHER CHEMICAL GROWTH REGULATORS IN ANIMAL PRODUCTION

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SUMMARY

Growth promotants are extensively used in animal production systems. The growth promotant action of hormonal growth promotants and beta adrenergic agonists and their role in animal production in terms of total weight gain (TWG), feed conversion efficiency (FCE) and carcase characteristics are reviewed. Under the right conditions oestrogenic, progestagenic and androgenic hormonal growth promotants (HGPs) are effective in cattle and sheep. They appear to be of no benefit in pig production. Somatotrophin is emerging as an effective growth promotant in pigs, cattle and sheep. The beta adrenergic agonists appear to have potential as growth promotants in cattle and sheep but not in pigs. Availability of suitable feed is critical to obtaining a good growth response to HGPs. In cattle under pasture conditions development of a treatment regime must ensure that feed quality and quantity is adequate otherwise the benefits of using HGPs will not be realised. The future use of growth promotants is considered and it is concluded that they will continue to have a role in improving TWG, FCE and carcase composition. However, the type of growth promotant used in the future will be determined by issues relating to consumer health and animal welfare as well as production economics.

INTRODUCTION

Hormonal growth promotants (HGPs) and other chemicals with growth promotant effects are increasingly being used to maximise production and improve productivity in animal production systems. This is achieved by increasing total weight gain (TWG), increasing food conversion efficiency (FCE) and improving carcase characteristics. Their introduction to agricultural production was a natural progression alongside improved management of livestock nutrition and the implementation of breeding programs aimed at improving the carcase quality and productivity in livestock production. Today they are used widely in both intensive and pasture based production systems.

Growth promotants may act by directly influencing the metabolism of the animal, modifying the microbial flora of the gastrointestinal tract and by improving the 'overall health of the animal. Metabolic actions may involve the laying down of more protein and fat, more efficient use of protein and a reduction of the relative proportion of carcase fat. Modification of the gastrointestinal microflora by antibacterial agents is claimed to improve availability of those nutrients required for growth and development.

Hormones currently used in Australia as growth promotants are the naturally occurring oestrogenic, progestagenic and androgenic steroids and synthetic compounds with similar action. Zeranol available under the trade name Ralgro is a xenobiotic with oestrogenic activity. It is produced from the naturally occurring product zearalenone. The synthetic anabolic steroid trenbolone is commonly used overseas as a growth promotant and is expected to be available commercially in Australia in the near future.

Natural and synthetic HGPs have been shown to be effective in beef cattle under pasture conditions and in lot-feed systems in Australia (Hodge et al., 1986; Mason, Rudder and Burrow 1986; Hamilton and Seier 1988; Sawyer et al., 1988) and overseas (Brown 1983; Reid 1983). In overseas countries HGPs are also

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widely used in pigs and sheep. In some overseas countries growth hormone or somatotrophin has been used as a growth promotant. Somatotrophins are not yet available as growth promotants in Australia.

Beta adrenergic agonists such as clenbuterol and cimaterol have emerged as growth promotants in a number of overseas countries. These chemicals are not registered for use as growth promotants in Australia.

A wide range of antimicrobial compounds are commonly used as growth promotants in livestock production systems. Antiprotozoal and anthelmintic agents are also used (O’Connor 1980; Broome 1980).

Antimicrobial agents used as growth promotants cause beneficial changes to the ruminal or intestinal microflora which improve nutrient availability. They also remove pathological organisms increasing the overall health of the wall of the gastrointestinal tract and the animal in general (Hooke 1973; Broome 1980; O’Connor 1980). The use of antimicrobial growth promotants may also result in an increase in the synthesis of vitamins and other growth promoting factors by the intestinal microflora (Shahani and Whalen 1986). Direct effects of antimicrobial chemicals on the levels of circulating growth factors have been suggested as contributing to their growth promotant effects however these effects are more likely to be related to the changes to the microflora (Coates 1980; O’Connor 1980).

In ruminants modification of the rumen microflora by compounds such as monensin results in increased propionate production in the rumen and increased availability of nitrogen to the animal from plant rather than microbial sources (Broome 1980). Higher levels of propionate in the rumen allow gluconeogenesis to proceed with less reliance on amino acid breakdown as the energy source leaving the amino acids more readily available for protein production.

Despite the value of growth promotants in animal production there are serious public concerns about the public health and animal welfare implications of their use. Without doubt these public perceptions about the use of growth promotants will shape the future of growth promotants in animal production. The decision by the European Council of Agricultural Ministers to introduce legislation prohibiting the use of HPGs in member countries of the European Community (EC) is an example of the influence of public opinion on these issues. This decision was taken despite ample scientific evidence that the products were efficacious as growth promotants and that they presented no human health risks (Enright 1988).

The EC decision to ban HPGs has had a significant impact on Australian animal production. All livestock treated with hormones for growth promotant purposes are not permitted to be used for production of meat or offal destined for the EC. Maintaining the integrity of product has resulted in complex administrative systems of considerable inconvenience to producers, livestock marketing systems and processors.

This paper reviews the mechanism of action of the various hormones and beta agonists used as growth promotants and their role in animal production in terms of total weight gain, feed conversion efficiency and carcase characteristics. The future role for growth promotants is also considered.

**HORMONAL GROWTH PROMOTANTS**

In-the main HPGs act by directly influencing protein and fat metabolism and by creating a negative feedback effect on the production and/or release of naturally occurring sex hormones in the animal. The effect on protein and fat metabolism also results in increased FCE in cattle, lambs and pigs.
Somatotrophin or growth hormone directly influences growth and development of the animal in the same way as it does naturally. FCE, TWG and carcass composition may be improved by the use of somatotrophin (Bryan et al. 1987; Etherton et al. 1987; Campbell et al. 1988; Evock et al. 1988; Enright 1989; Zainur et al. 1989).

The use of porcine somatotrophin in pigs has been shown to improve FCE by 17 percent (Etherton et al. 1987), 20 percent (Evock et al. 1988) and 23 percent (Campbell et al. 1988). The improvement in FCE appeared to be dose related and was 7, 10 and 17 percent respectively for doses of 10, 30 and 70 ug/kg body weight/day (Etherton et al. 1987).

Corresponding increases in growth rate and TWG of up to 20 percent and 7 percent respectively were reported. The growth rate increased up to a dose rate of 35 ug/kg body weight/day after which no further increase was observed (Evock et al. 1988). Despite this upper limit to the dose response of growth rate higher dose rates continued to improve FCE and produce changes to carcass composition.

Somatotrophin produces significant changes to carcass composition in pigs. An increase of up to 50 percent in protein deposition has been reported (Campbell et al. 1988). Reduced carcass fat content and fat measurements also occur (Campbell et al. 1988; Evock et al. 1988). Fat accretion continues to reduce as the dose rate is increased (Evock et al. 1988). Gilts exposed to prolonged use of porcine somatotrophin at 70 ug/kg body weight/day were extremely lean (Bryan et al. 1987).

In lambs similar benefits in terms of FCE, TWG and carcass composition can be obtained by using somatotrophin (Enright 1989; Zainur et al. 1989). Increases in growth rates of up to 45 percent, a 29 percent improvement in FCE, a 16 percent increase in carcass protein and a significant reduction in the amount of subcutaneous fat present in treated animals were reported by Zainur et al. (1989).

Cattle treated with somatotrophin also respond with increased TWG, FCE and carcass lean in conjunction with reduced carcass fat (Enright 1989). In Australia a trial in immature grazing cattle showed a 7.6 percent increase in growth rate and a 17 percent decrease in carcass fat (Sandles 1986).

In heifers and pigs, treatment with somatotrophin releasing hormones or synthetic analogues has been demonstrated to be effective in increasing the release of somatotrophin (Petitclerc et al. 1987; Scarborough et al. 1988). This could be a viable alternative to the use of somatotrophin.

Oestrogen, testosterone and progesterone

The natural sex hormones oestrogen, testosterone and progesterone or synthetic analogues have been used individually or in combination to produce improvements in FCE, TWG and carcass composition in cattle and sheep (Reid 1983; Wagner 1983).

Selection of the combination to be used in cattle relates to the sex and age of the animal. As a general rule the selection is based on achieving a balance between those hormones which naturally occur at high levels in the animal and those which do not. Combinations of oestradiol and progesterone are generally used in steers and bulls whereas combinations of oestradiol and testosterone are generally used in heifers and cows (Reid 1983). Either combination is used in suckling and veal calves.

In overseas trials lot-fed steers treated with oestradiol and progesterone
Implants showed an average daily gain (ADG) 10 to 50 percent above that of controls whereas for pasture-fed steers the range was 15 to 30 percent above controls (Reid 1983). Oestradiol alone used in steers will produce an 8 to 32 percent increase in growth rate (Wagner 1983). These findings are consistent with trials conducted in Australia which demonstrated a 15 percent increase in ADG in lot-fed steers treated with oestradiol and progesterone implants (Sawyer et al. 1988) and a 22 percent increase in ADG in 18 month old pasture-fed steers treated with oestradiol implants (Mason, Rudder and Burrow 1986). Backfat thickness did not vary from that of the controls in the Australian trials, indicating that there are no major changes to carcase quality. The dressing percentage in Australian lot-fed steers increased by an average 1 percent with one implant and 1.4 percent with two implants, the second being administered 42 days after the first (Sawyer et al. 1988).

Overseas trials using heifers demonstrated an increase in ADG of 14 to 24 percent in lot-fed heifers and 6 to 25 percent in heifers at pasture when treated with oestradiol and testosterone (Reid 1983). Under Australian conditions lot-fed heifers implanted with oestradiol and testosterone have shown a 15 percent increase in ADG (Sawyer et al. 1988). Changes in carcase backfat thickness and dressing percentages in the Australian trials were similar to those observed for steers.

The improvement in ADG observed in bulls treated with oestradiol and progesterone implants ranges from 3 to 15 percent (Reid 1983), which is considerably less than that reported for steers. However, the same author noted that carcase changes are significant in that there is an increase in the amount of fat in the carcase and an improvement in carcase conformation with multiple implant regimes commencing at an early age. Oestradiol used in bulls also reduces testicular size considerably when multiple implant regimes are used (Reid 1983).

Prior to the EC decision to ban HPGs, implants of natural hormones and synthetic analogues played an important role in veal production in Europe. The intensive nature of this industry has required producers to maximise the use of production aids such as growth promotants. Increases in ADG of around 10 percent have been reported for intensively raised veal calves treated with implants containing oestradiol and progesterone or oestradiol and testosterone (Reid 1983). Similar responses were reported in suckling calves. In calves the amount of oestradiol in the implant is half that used in older cattle.

Extremely variable results have been noted when these hormones are used in pigs. An increase in the lean to fat ratio has been observed in all pigs except boars (De Wilde and Lauwers 1984). In the case of boars treated with oestradiol no increase in carcase fat content was observed. These authors also noted that treatment of pigs with combinations of oestradiol with progesterone and oestradiol with testosterone generally had negative effects on TWG. The only group showing a positive response were gilts treated with oestradiol and testosterone. No effect on FCE was observed. Other authors have reported no real benefits in using oestradiol or testosterone in castrated male pigs under 6 months old (Chaudhary and Price 1987).

Zeranol

Zeranol has been shown, in overseas trials, to increase TWG and FCE in veal calves, steers and bulls (Brown 1983). Increases in TWG after treatment with zeranol have been observed in lot-fed steers and heifers in Australia (Hodge et al. 1986; Sawyer et al. 1988). The use of zeranol to increase TWG in pasture-fed cattle in Australia has also been shown to be effective (Hodge et al. 1983; Mason et al. 1986; Hodge et al. 1986). The increase in TWG associated with the use of zeranol in all cattle other than entire males is not accompanied by an increase in carcase fat (Brown 1983; Sawyer et al. 1988).
The benefits of using zeranol in young calves appear to be significant. In northern Victoria an increase in growth rate of up to 30 percent was observed in calves born in early summer and implanted with zeranol 3 months before slaughter (Hamilton and Seirer 1988). The increase in carcass weight was accompanied by a decrease in carcass fat thickness. Similar benefits have been observed in Europe and the USA (Brown 1983). The response of suckling calves, however, is feed dependent. When forage nutrition and maternal milk flow were below optimal conditions suckling calves failed to respond to implanting with zeranol (Sims et al. 1988).

There are conflicting views on the benefits of using zeranol in entire male cattle. In a Canadian trial, bulls receiving 4 implants at 84 day intervals the first at 55 days old showed a slight but insignificant increase in TWG (Richards et al. 1987). Carcass changes in these bulls were also only considered slight. The authors did, however report that there was a definite reduction in testicular size.

One set of trials in the USA demonstrated a higher ADG in non implanted bulls under 12 months old with the implanted bulls showing the highest ADG after 12 months of age (Gray et al. 1986). These authors also reported increased carcass fat thicknesses and a reduction in the rib eye areas per 100 kg of carcass. This is consistent with an oestrogenic effect in bulls.

Other trials in the USA and Europe using zeranol in bulls have reportedly resulted in increases in ADG (2% to 23%) and FCE (3.3% to 7.3%) as well as more fat cover and an increase in the eye muscle area (Brown 1983). These results included a UK trial in which bulls less than 12 months old showed an increase in ADG of 14.7 percent and an improvement of 4.8 percent in FCE after lot feeding using cereal and concentrate rations.

The apparent influence of age is probably due to the variation in the levels of natural hormones in the bull at the various stages of sexual development. The variation in plane of nutrition in the UK trial may have accounted for the different response, highlighting the importance of feed quality and availability in realising the benefits of HGPs.

Benefits arising from the use of more than one implant in the same animal are variable. Trials under pasture conditions in Colombia, South America, showed that a second implant of zeranol 90 days after the first resulted in a further improvement in TWG over that of a single implant (Brown 1983). Considerable benefits derived from the reimplantation of bulls were also reported by that author. However, the use of multiple implants was investigated under Australian conditions near Rockhampton in Queensland and it appeared that long term use of zeranol and other HGPs offered no benefits over their use during the final 200 days before sale or slaughter. The absence of any real benefit from the long-term use of zeranol has also been suggested by researchers in the USA (Mader et al. 1985; Sims et al. 1988).

Trenbolone

Trenbolone is an anabolic steroid which has been demonstrated to improve TWG, FCE and carcass quality in cattle. It is a potent androgen and is generally used in conjunction with oestradiol.

Australian trials using two groups of pasture-fed steers and two groups of lot-fed steers have demonstrated that trenbolone in combination with oestradiol increased ADG by 40 and 70 percent in the steers at pasture and by 19 and 40 percent in the lot-fed groups (Hodge et al. 1986). The four trials conducted compared the use of trenbolone and oestradiol with that of zeranol. In all of the trials the increase in liveweight gain was considerably more than that observed with zeranol. These authors also reported side effects of masculine appearance including a pronounced neck crest which in the opinion of the...
Trenbolone in combination with oestradiol has also been trialled in lambs in Australia resulting in an increase of approximately 5 percent in TWG (D’Occhio et al. 1986). These authors also noted that treatment retarded pubertal development in ram lambs by suppressing gonadotrophin secretion. It was suggested that implants of trenbolone and oestradiol may have a role as an alternative to castration.

Trenbolone has also been shown to improve metabolic efficiency of cattle on low quality roughage diets resulting in reduced weight losses in treated cattle (Hunter and Vercoe 1987). The use of trenbolone to reduce weight loss in cattle during the dry season in Northern Australia is being investigated by the Commonwealth Scientific and Industrial Research Organisation, Division of Tropical Animal Production. Treatment with oestradiol and testosterone does not appear to reduce weight losses in cattle fed poor quality diets (Hunter and Vercoe 1988; Hunter 1989).

**BETA ADRENERGIC AGONISTS**

The beta adrenergic agonist group of chemicals are repartitioning agents which modify fat and protein metabolism in the animal. Protein accretion and hypertrophy of muscle fibres occurs with the use of beta agonists (Kim, Lee and Dalrymple 1987). These authors also reported that the extent of muscle hypertrophy was considerably greater in Type II fibres than Type I fibres. Beta agonists have a dual role in lipid metabolism in that they stimulate lipolysis as well as depressing lipogenesis (Peteris, Ricks and Scanes 1987).

Clenbuterol administered to lambs has been shown to improve FCE and carcass quality (Baker et al. 1984). The use of cimaterol, an analogue of clenbuterol, reportedly resulted in a 14 percent increase in FCE and a 29 percent increase in TWG in lambs (Kim, Lee and Dalrymple 1987). These authors also reported a 38 percent increase in the cross-sectional area of the longissimus dorsi muscle with the area of Type II muscle fibres increasing by approximately 50 percent. This was achieved by including cimaterol in a high concentrate diet at the rate of 10ppm. Similar increases in muscle size of lambs were reported in other trials using cimaterol as a growth promotant (Beermann et al. 1987).

In heifers treated with clenbuterol considerable improvements in carcass quality have been reported (Miller et al. 1988). Of particular interest was the observation that subcutaneous fat deposits were reduced compared with the controls and intramuscular fat deposition was similar. This would indicate that the influence of beta agonists on lipogenesis and lipolysis is site specific. These authors also reported a 20 percent increase in the size of Type II muscle fibres and no effect on Type I fibres. Similar responses in terms of carcass composition have been obtained with steers (Duquette et al. 1987). The steers also showed a 4 percent increase in TWG and a 33 percent increase in FCE.

There appear to be no benefits in feeding pigs beta agonists as growth promotants. Results of trials using cimaterol have demonstrated no benefits in terms of TWG but improved carcass characteristics and FCE (Jones et al. 1985). The improved FCE was accompanied by depressed feed intake resulting in no increase in TWG. Cross-sectional areas of major muscle groups were increased by approximately 10 percent and backfat thickness was reduced by 10 percent. An important observation was that withdrawal of cimaterol resulted in a rapid deposition of fat, the backfat thickness increasing to match the controls within 7 days. Other authors did not observe significant variations in TWG, FCE or carcass characteristics (Mersmann et al. 1987).
The foregoing clearly shows that growth promotants have the ability to improve TWG, FCE and carcass composition and as such have a role in animal production systems. However, the response is extremely variable and, depending on the availability and quality of feed, species, sex, age and the overall health status of the animal, there may be no benefits from their use. These factors as they relate to the production system and the type of growth promotant must be considered carefully in the selection of growth promotant(s) to be used.

With the exception of somatotrophins, there are no apparent benefits to be derived from the use of hormones and beta agonists as growth promotants in pig production. Should somatotrophins become available for use as HGPs in pig production in Australia, the treatment should be selected on the basis of the extent to which carcass lean content is important. This is because the lean to fat ratio increases as the daily dose increases whereas improvements in TWG increase initially but plateau at an upper daily dose (Evock et al. 1988).

In cattle and sheep HGPs and beta agonists appear to be effective growth promotants providing they are used under favourable conditions. To obtain maximum benefit from their use, it is very important to select an HGP most suited to the species and sex of the animal to be treated. Manufacturers of products available in Australia provide details with the product.

Development of a treatment regime for the use of HGPs requires a careful analysis of feed availability and management objectives in terms of the product required. Given the variability in response of animals to HGPs it would seem that on-farm trials to identify the optimum time to use HGPs and the most suitable product to use are needed. In fact the variation in response to growth promotants in general would indicate that properly conducted on-farm trials and the keeping of accurate on-farm records of product performance should be undertaken at the producer level to optimise growth promotant use.

Consumers are currently demanding leaner meat and at the time of purchase visible lean is most important. In cattle and lambs somatotrophin and beta agonists have the potential to provide the carcass characteristics currently being demanded by consumers. Use of somatotrophin in pigs, particularly the higher dosage treatment regimes, also achieves this aim.

The role of growth promotants in animal production is unlikely to change in the short to medium term. However, the chemicals used will most likely change to natural products or synthetic chemicals closely resembling them. This will result from consumer pressure brought about by human health and animal welfare concerns.

In the not too distant future HGPs available now will be replaced by slow-release somatotrophin implants. These will probably be superseded by the introduction of highly potent analogues of somatotrophin releasing hormone available in slow-payout formulations.

Further away is the production of transgenic animals producing increased levels of somatotrophin or somatotrophin releasing hormone. Projects to produce transgenic pigs along these lines are already underway (Pinkert et al. 1987). The economic benefits of not having to treat the animals will encourage producers to use transgenic animals in the long term.

The use of antimicrobials as growth promotants may decline with the introduction of probiotics to modify the intestinal microflora. Probiotics which are effectively a culture of yeast and bacteria are already available in other countries. They reportedly improve TWG and FCE considerably in pigs and...
calves (Chapman 1988; Williams 1988).

We have already seen the impact of consumer pressure on HGPs in the EC where their use is now prohibited. The original ban has now been extended to cover virtually all chemicals which have a direct effect on metabolism and which may be used in an attempt to promote growth given that no legitimate HGPs exist. Over time this attitude will undoubtedly permeate other countries and will extend to most, if not all, growth promotants, leaving their future in the hands of politicians rather than animal production and human health experts.

In conclusion the role of growth promotants is and will continue to be to improve TWG, FCE and carcass composition. However, the type of growth promotant used in the future will be determined by issues relating to consumer health and animal welfare as well as production economics.

REFERENCES


