



Types and Uses of Growth Promoters in Beef Cattle

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Abstract

Growth promoters are substances that are added to feeds as supplement or injection to improve feed utilization and growth of farm animals. Cattle producers use growth promoters to increase growth rates and improve overall efficiency and product quality. The most extensively applied growth promoters are feed additives, anabolic implants (both estrogenic and androgenic), bovine somatotropin, β -agonists and probiotics. All non-nutrient feed additives such as antibiotics and exogenous enzymes that improve animal growth can be described as growth promoters. Hormonal growth promoters have generated various positive effects in cattle production; such as, prevention and treatment of animal diseases, and enhancement of animal production. However, hormonal growth promoters may cause carcinogenic effect to the consumer. Unable to adhere to the guideline of probiotic production may lead to the development of pathogenic organisms. Human health can either be affected directly through residues of an antibiotic in meat, which may cause side-effects, or indirectly, through the selection of antibiotic resistance determinants that may spread to a human pathogen. Some of the antibiotics used for growth promotion in pigs, poultry and/or cattle are classified by the World Health Organization as critically important antibiotics for use in human medicine. These conditions favor the selection and spread of antibiotic resistant bacteria among animals, to the environment and eventually to humans. Thus, the objective of this review was to access the types and uses of growth promoters in beef cattle.

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Introduction

The benefits and risks of growth promoters continue to be complex and controversial issues. The risks of antimicrobial drugs to public health associated with antimicrobial resistance raised great concern recently, while the benefits of antimicrobial drugs, such as prevention and treatment of animal diseases, protection of public health, enhancement of animal production, and improvement of environment, were disregarded most of

the time. Many benefit-related claims have not yet been fully demonstrated in large-scale trials, and other trials revealed that the overall impact of the short-term benefits was poorly described. This article presents the benefits and risks of antimicrobial drugs used in food animals and discusses the positive and negative effects of the ban on antimicrobial growth promoters [1].



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Application of growth promoters by means of supplementation to the diets has been routine in the beef cattle industry of many countries for the better performance in growth and improvement of feed efficiency. Anabolic implants (zeranol, trenbolone acetate, and estradiol with testosterone or progesterone) have generated various positive effects. Zeranone implantation, in general, improved average daily gain, feed conversion, Dressing Percentage (DP) and Yield Grade (YG) of cattle, and increased dry matter intake [2]. Trenbolone acetate with or without estradiol also increased mean values of average daily gain and loin eye area but reduced dry matter intake and improved feed conversion of cattle. Estradiol with testosterone or progesterone increased average daily gain and dry matter intake. Anabolic implants, however, had minimal or negative effects on marbling or quality grade. The magnitude of the response to these anabolic implants in performance of beef cattle has varied depending on the type of implants, amount and duration of exposure, age of animals and combination of implants. Administration of bovine somatotropin improved ADG and FC, and decreased fat deposition. Ionophores improved FC in cattle from reduced DMI without great response to ADG [3]. Supplementation of monensin and lasalocid reduced molar proportion of propionate. Monensin and lysocellin increased apparent absorption and retention of some minerals in cattle. Even with the improved cattle performance in growth and FC, results in beef quality from the application of the growth promoters appeared to vary or in conflict under a variety of environmental conditions [4]. Thus, the need to compile this review was to access the types and uses of growth promoters in beef cattle.

Growth promoters used in beef cattle

Growth promoters are substance used to increase the feed conversion efficiency, average daily gain and carcass quality or milk production of animals. Both genetics and nutrition are the two most important factors affecting animal productivity. Meat animal producers are concerned with the amount of protein fed that is converted into muscle deposition. Protein formation can be estimated by comparing the amount of nitrogen fed to the amount of nitrogen in the animal's waste. However, growth promoters can improve the efficiency of animals to use nitrogen of their ration to form amino acids and build their own protein. Most growth promoters accelerate nitrogen retention in the body [5].

Types of growth promoters

Beef Cattle growth promoters are divided into five groups as feed additives, hormonal implants, growth hormone (Somatotropins), beta-agonists and probiotics [6]. The characteristics of each are as follows:

Feed additives

A feed additive is a substance added to feed to fulfill a specific need of the animal. The additive may provide a needed nutrient or increase an animal's resistance to disease. Many feed additives were available such as antibiotics, organic acids and exogenous enzymes. These compounds will be added to the milking and fattening diet of farm animals to improve the growth performance, nutritional parameters and carcass traits [7]. Antibiotics used as feed additives, develop their activity in the digestive tract of animals by suppressing the undesired competitive microorganisms that utilize nutrients and produce undesirable or toxic substances resulting in an optimal environment for the intestinal mucosa, which allows an efficient nutrient absorption. Therefore, nutrient utilization, feed conversion

ratio and growth rate improved [8] also indicated that growing animals will get maximum benefits from antibiotic growth promoters (AGPs). Antibiotic growth promoters demonstrated low resistance capacity at authorized use levels includes Monensin, Flavomycin and Virginiamycin [9].

From the advantages of Monensin and Ionophore group of antibiotics are used only in agriculture [10]. It has no equivalent products used in human medicine, or even share a mode of action with any compound in human medicine and do not have antibiotic resistance encoded by transferable genes Monensin acts on bacteria by facilitating the carriage of sodium ions into the cell to speed up the sodium/potassium pump in the cell membrane leading to ion imbalance. As the transport mechanism requires energy in the form of Adenosine Triphosphate (ATP), continuous exposure to Monensin could lead the cell to exhaust energy supplies, resulting death by osmotic disruption of the cell, but more usually it prevent formation can be estimated by comparing the population and their numbers decline [6].

Hormonal implants

Implanting hormonal growth promoter is currently widespread in the beef cattle industry of many non-EU countries for the better performance in growth and improvement of feed efficiency. These hormonal implants may enhance growth during suckling, growing and finishing stages of meat production [11]. They are implanted under the skin (usually behind the ear) of the animal in the form of depot capsules, where they release a specific dose of hormones over a fixed period of time. Types of hormones most widely used in cattle production in the form of implant include natural hormones, (estradiol, testosterone and progesterone) and synthetic ones (trenbolone acetate and zeranol). Estradiol has responsible for female characteristics, testosterone has responsible for male characteristics, and progesterone has responsible for maintaining pregnancy. The other two hormones mimic the biological activity of the natural hormones: trenbolone acetate mimics the action of testosterone and zeranol mimics' estradiol [12]. Estradiol promoted growth by stimulating appetite and improving FCE. Testosterone or testosterone propionate, alone or in combination with other hormonally active substances, used primarily to improve the rate of weight gain and feed efficiency by anabolic action of androgens. It is well established that progesterone not only serves as the precursor of all the major steroid hormones (Androgens, oestrogens, corticosteroids) in the gonads and adrenals, but also is converts into one or more metabolites by most growth rate of animal [13]. Trenbolone Acetate (TBA) is a synthetic steroid with an anabolic potency that may exceed that of testosterone. It is assumed to exert its anabolic action via interaction with androgen and glucocorticoid receptors including bile. It is assumed to exert its anabolic action via terbutaline and zilpaterol. Zilpaterol, present as an active interaction with androgen and glucocorticoid receptors Zeranone is derived from the naturally occurring myco estrogen zearalenone and is a potent estrogen receptor agonist *in vivo* and *in vitro* [14]. Its actions resemble those of estradiol and used alone or in combination with TBA as a hormonal growth promoter in various products [15].

Growth hormones

Growth Hormone (GH) is a single polypeptide chain consisting of 191 amino acids, varying considerably between species. It increases weight gain by stimulates metabolism and protein accretion concurrent with a reduction in fat deposition [16].

Bovine Somatotrophine (BST) is a bovine growth hormone produced by the pituitary gland of the cow. This hormone is a protein, like insulin, not a steroid hormone, such as sex hormones or cortisone. During lactation, BST mobilizes body fat for use as energy and diverts feed energy towards milk production rather than tissue synthesis. In fact, BST increases efficiency in milk production by 10% to 15% [17]. Though the use of BST is primarily concentrated on increasing milk product its effects on beef cattle are increased growth rates, improved feed conversion and carcass lean, while decreasing carcass fat. The effect on eating quality of the meat associated with reduced carcass fat is a reduced acceptability because of lower scores on tenderness [9].

Repartitioning agents (β -Agonists)

Beta-adrenergic agonists enhance growth efficiency by stimulation of beta-adrenergic receptors on cell surfaces. They act as repartitioning agents to modify carcass composition by altering nutrient partitioning to lower fat deposition up to 40% and increase muscle protein content up to 40%. Increased protein accretion is mediated by binding of the agonist to muscle 1 and 2 receptors, leading to increased muscle protein synthesis. In muscle tissue, beta-agonists promote protein synthesis and cell hypertrophy by inhibition of proteolysis. In adipose tissue, beta-agonists promote lipolysis. They may have a secondary mechanism mediated by other hormones by increasing blood flow.

A wide range of compounds has been investigated as beta-agonists including cimaterol, clenbuterol, fenoterol, isoprenaline, mabuterol, ractopamine, salbutamol, terbutaline and zilpaterol. Zilpaterol, present as an active beta2-agonist in Zilmax, is one of the new beta agonists officially registered for fattening purposes in cattle in Mexico and South Africa. Zilpaterol hydrochloride is a powerful beta agonist, which is more effective than ractopamine, but only about one-tenth effective as clenbuterol. Mexican reported that zilpaterol supplementation can have a marked beneficial effect on growth performance and carcass yield of feedlot steers. Enhanced growth performance accounts for 55% of the net economic value of zilpaterol supplementation (Benefit to the feeder), while increased carcass cut ability accounts for 45% of the net value (benefit to the meat packer and retailer) [17]. When beta-agonists are used as growth promoters, two major problems arise during chronic exposure.

Firstly receptor down regulation leads to a falloff in effect over time and a 'rebound' when the product is removed, leading to an increase in fat deposition and a reduction in muscle mass. The most effective use of a repartitioning agent is therefore in the finishing period in the one to two months prior to slaughter [6].

Probiotics

Probiotics are mono or mixed culture of living microorganisms, which induce beneficial effect on the host by improving the properties of the indigenous microflora [18]. Several microorganisms have been considered as probiotics including fungi particularly mushroom and yeast, bacteria and mixed cultures comprising of various microbes [19]. Bacteria are more commonly reported as probiotic than fungi. The microorganisms used as probiotics are indicated in Genera *Lactobacillus* [20] and *Bifidobacteria* [21] are mostly reported. Other bacteria that have been used, to a lesser extent in poultry and animal probiotics include *Bacillus*, *Enterococcus*, *Streptococcus*, *Lactococcus*, *Pediococcus* and *Selenomona scerevisiae* [17].

Benefits of growth promoters in beef cattle

Prevention and treatment of animal diseases

With intensive animal production, bacterial and parasitic diseases became more and more frequent. According to an estimate, 80 types of bacteria, such as *Escherichia coli*, *Salmonella*, and *Clostridium* are involved [22]. Due to infection caused by *Streptococcus pneumoniae*, morbidity and mortality rates in calves increased to 40% and 20%, respectively. More than 50% of aquatic animals were infected by bacteria each year [23]. Many antimicrobials have strong activity against parasites in animals. Use of sulfonamides in animals opened a new era of anti-parasitic drugs and made lots of parasitic diseases under control. Up dig now, anti-parasitic drugs have shared about one-third sale of the global veterinary drug markets. Macrolides and benzimidazoles effectively controlled nematodes. Doramectin and Ivermectin helped to prevent infection of *Argulus siamensis* in carp and *Labeo rohita*. Conclusively, due to unique advantages, such as exact targeting of pathogens, well-known mechanisms of activity and desired stability, antimicrobials justified their usage in livestock and poultry, and played important part for prevention and treatment of bacterial and parasite diseases [24].

Enhancement of animal production

Role of antimicrobials for the improvement of feed conversion ratio (FCR), animal growth, and reproductive performance has been well proven administration of antibiotics (bacitracin zinc, colistin sulfate, flavomycin, and florfenicol) in fish diet significantly improved the feed conversion and promoted their growth [25]. Antimicrobial (tiamulin, nosiheptide, salinomycin, and tylosin) supplementation could also improve the carcass quality by decreasing the fat thickness and increasing the lean meat of food-producing animals [26]. Dig now, there are no appropriate alternatives which can replace antimicrobial growth promoters, in case those remain banned. Although numerous feed additives, mainly pre and pro-biotic products, are commercially available now and seem to have potential to replace these growth promoters, but their true efficacy and mechanism of action in domestic animals remain unclear because of some inconsistent experimental results [18]. Additionally, lack of safety evaluation and poor stability also limited the practical use of pre and pro-biotic as feed additive [27] antimicrobials have multi-functional role in animals, elaborated under following points: (1) these could reduce the colonization of intestinal bacteria and inhibit the growth of pathogenic microorganisms; (2) by decreasing the thickness of mucous membrane, led to more absorption of nutrients and reduced fermentation; (3) they directly neutralized the host immune response. In short, antimicrobials could affect the host intestinal flora, intestinal physiology, and immune system, and consequently, prevent disease, improve feed conversion, and enhance the growth of animals [28].

Improvement of environment

Housing stress, due to over-crowding of animals, creates sweeping and devastating impacts on the natural and human environment leading to global warming, land degradation, air and water pollution, and loss of biodiversity. Livestock waste is one of the major sources of greenhouse gases, as the abnormal fermentation of gastrointestinal tract contents can produce lots of methane, ammonia, carbon dioxide, as well as stench gases nitrogen and phosphorus in the waste lead to environmental

pollution, water eutrophication and ecological imbalance. Some antimicrobials in feed could inhibit the abnormal fermentation and consequently, reduce the emission of greenhouse gases (mainly CH₄) [37]. Ionophorous antibiotics have been widely used as feed additives in ruminants due to their favorable effects on rumen fermentation and methane reduction [29]. Due to the efficacy and affordable price, ionophores have widely been used to reduce methane emission from livestock more food animals should be raised to meet the food supply demand in the case of growth-promoting antibiotics remain prohibited and this increased number of animals will again lead to the increase in greenhouse gas emission and deeper environmental pollution [29,30].

Impact of growth promoters in beef cattle

Inhibition of biogas production

The wide use of antimicrobial drugs in intensive animal production for growth promotion and prevention or treatment of disease, a large proportion of ingested drugs are excreted in manure and end up with livestock waste water. Excreted antibiotics in the environment may partially inhibit methanogenesis in anaerobic waste storage facilities, commonly used at Concentrated Animal Feeding Operation (CAFOs), and thus, decrease the rate at which bacteria metabolize animal waste products. During the anaerobic digestion of livestock waste, certain antimicrobials, including amoxicillin, aureomycin, oxytetracycline, thiamphenicol, florfenicol, sulfadimethoxine, and tylosin, had inhibitory effects on methane production [31]. Biogas volume, produced from per unit weight of biomass, was decreased with increasing concentrations of antibiotics, such as oxytetracycline, amoxicillin, and tylosin, and the inhibitory concentrations of oxytetracycline, amoxicillin, and tylosin were 8000, 9000, and 9000 mg/L, respectively [32].

Antimicrobial Resistance Concerns

Misuse and overuse of antimicrobial may end in the development of drug-resistant pathogens resulting in poor response to treatment. Long-term and low-level exposure to antimicrobials may have greater selective potential than short-term and full-dose therapeutic use. A study observed that the percentage of tetracycline resistance genes in the fecal flora of conventionally raised feedlot steers was significantly higher than that in fecal samples from antimicrobial-free cattle. Additionally, use of single antimicrobial may induce cross-resistance to antimicrobials used for animal and human medical therapy. For example, chlortetracycline use in growth rations was associated with ampicillin and tetracycline resistance in generic fecal *E. coli*. Therefore, how to use antimicrobials, for effective treatment of bacterial and parasitic infections in food-producing animals, became the most important question for their use by avoiding the resistance development [33]. The resistant bacteria may also be released into the environment by humans and then transferred into new hosts in the environment [34-36]].

Conclusion

Growth enhancing compounds, including steroidal implants and β -adrenergic agonists, increase production and improve feed efficiency of beef cattle. The changes in performance result in an economic benefit to beef cattle producers and impact the relative price competitiveness of beef as compared to other dietary protein sources. Long-term use of growth enhancing technologies has proven that the compounds are a safe and effective way to enhance lean-tissue deposition in cattle. The compounds

are rapidly metabolized and excreted from the animal, assuring no risk of potential residues in the edible tissues. The safe use of growth enhancing compounds benefits the consumer. First, consumers benefit from the reduced production cost associated with the use of this technology in beef production. Second, consumers benefit from the improved lean protein options through beef from cattle reared with growth-enhancing technologies. Beef cattle growth promotion products, when used consistent with their label, are safe for the animal, the beef consumer, the environment and deliver significant economic benefits to the beef producer and to the consumer.

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