Advances in Biological Research 11 (1): 24-34, 2017
ISSN 1992-0067

DOI: 10.5829/idosi.abr.2017.24.34

Growth Promoters in Cattle

Tamirat Herago and Abebe Agonafir

Jigjiga University, College of Veterinary Medicine, Ethiopia

Abstract: Growth promoters are substances that are added to feeds as supplement or injection to improve feed utilization and the 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, repartitioning agents (Beta-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 (Zeranol, trenbolone acetate and estradiol) have generated various positive effects in cattle production. 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. On a global level, a recent joint workshop was held involving the World Health Organization, Food and Agriculture Organization of the United Nations and the World Organization for Animal Health on non-human antimicrobial usage and antimicrobial resistance. The resulting report recommends implementation of the World Health Organization as global principles for the containment of antimicrobial resistance in animals intended for food.

Key words: Antibiotics · Beta Agonists · Growth Hormones · Growth Promoters · Probiotics

INTRODUCTION

Growth promoters are substances that are added to feeds as supplement or injection as drugs to improve feed utilization and the growth of farm animals. In areas where there is increasing trends of beef and milk demand growth promoters are very important to meet the human needs. The most extensively applied growth promoters are hormonal anabolic implants (Both estrogenic and androgenic), bovine somatotropin (BST), feed additives, Repartitioning agents (Beta-agonists) and probiotics [1]. All non-nutrient feed additives such as antibiotics and exogenous enzymes that improve animal growth can be principally described as growth promoters [2].

Many studies have been conducted to evaluate the effects of growth promoters on performances and carcass characteristics of cattle, aspects of endogenous hormonal and metabolites. Anabolic implants [3] and Bovine Somatotropin (BST) [4] are known to improve feed conversion efficiency (FCE) and growth rate (GR) by reducing fat deposition in cattle. Ionophores such as monensin could improve energetic efficiency in the cattle [5, 6] and lysocellin [7] affect mineral metabolism of ruminal bacteria. Steroids increased the weight gain in treated animals through net protein accretion and Nitrogen retention without any changes in the digestibility of Nitrogen intake [8].

However, most of these compounds have not gained widespread consumer acceptability and growth-promoting hormones were banned by the European Union (EU). The consequence of this EU position has leads to the development, in numerous countries, of a black market of hormone cocktails including potentially dangerous synthetic steroids and corticoids. Therefore, the objectives of this review were to give an overview on different types of growth promoters and its importance in

Corresponding Author: Tamirat Herago, Jigjiga University, College of Veterinary Medicine, P. O. Box: 1020, Jigjiga, Ethiopia
Tel: +251916133480.

cattle production, to indicate public health impact of growth promoters and to review policies on growth promoters used for cattle production.

Growth Promoters: Growth promoters are substances 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 [9]. 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 [10].

Types of Growth Promoters: Cattle growth promoters are divided into five groups as feed additives, hormonal implants, growth hormone (Somatotropins), repartitioning agents (β-agonists) and probiotics. The characteristics of each are discussed in the following sections.

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 [11]. 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 [12, 13].

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 [14]. Chen and Russell [15] 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 include Monensin [16], Flavomycine [17] and Virginiamycine [18, 19].

From the advantages of Monensin (an Ionophore a group of antibiotics that are used only in agriculture), 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 in death by osmotic disruption of the cell, but more usually it prevents the bacteria from competing in a mixed population and their numbers decline [20].

Rumen is a fermentation vat that converts carbohydrates into volatile fatty acids (VFAs) such as acetic, butyric and propionic acids that drive the animal's metabolites. The key to the efficiency of production of the VFAs is the preservation of the six carbons from the final fermentation substrate, usually a hexose sugar such as glucose. Propionic acid is only VFA that complete retention of all six carbon molecules in the fermentation products [21]. Monensin affects gram positive bacteria that produce acetic and butyric acid and creates suitable environments for propionate producing bacteria in the rumen [15]. Rumen active growth promoters have additional benefits in the control of acidosis [22], bloat control [23] and the prevention of coccidiosis [24].

The sensitivity of rumen bacteria to Monensin and their related products of fermentation are indicated in Table 1.

The AGPs with a more pronounced effect in the intestine are the Flavomycine and virginiamycine. Both of them inhibit the growth and metabolism of harmful gut bacteria, decreased elaboration of toxic substances, including bacterial toxins, reduced bacterial destruction of essential nutrients, increased synthesis of vitamins and other growth factors improve efficiency of nutrient absorption by modification of the gut wall, reduced intestinal mucosal epithelial cell turnover and reduce intestinal motility [26].

Organic acids are widely used to improve cattle performance through reducing the pH of feeds, digesta and creating negative conditions for microorganism growth and entering into the microbial cytoplasm to disrupt the life cycle of the microorganism, especially gram positives bacteria [19]. The combination of organic acids with certain types of essential oils obtained from herbal extracts had a synergistic effect on control of most bacterial growth, including *salmonellae*, *E. coli*, *Enterococcus, Staphylococcus* and *Clostridium* [18].

Table 1: The sensitivity of rumen bacteria to monensin and their related products of fermentation

Rumen Bacteria	Fermentation Products
Monensin-sensitive organisms	
Ruminococcus	Acetic acid
Methanobacterium	Acetic acid, methane
Lactobacillus	Lactic acid
Butyrivibrio	Acetic acid, butyric acid
Streptococcus	Lactic acid
Methanosarcina	Methane
Monensin-insensitive organisms	
Selenomonas	Propionic acid
Bacteroides	Acetic acid, Propionic acid
Veillonella	Propionic acid

Source: Chow and Russell [25]

Table 2: Some physiological, nutritional and metabolic effects of feed additive growth promoter

Physiological effects	Nutritional effects	Metabolic effects
Gut food transit time ↓	Nitrogen retention ↑	Amino production ↓
Gut wall diameter ↓	Energy retention ↑	Toxic amine production ↓
Gut wall length ↓	Limiting amino acid supply ↑	Alpha-toxin production ↓
Gut wall weight ↓	Vitamin absorption ↑	Fatty acid oxidation ↓
Fecal moisture ↓	Trace element absorption ↑	Fecal fat excretion ↓
Mucosal cell regress ↓	Fatty acid absorption ↑	Gut alkaline phosphatase ↑
Stress ↓	Glucose absorption ↑	Liver protein synthesis ↑
Gut absorption capacity ↑	Calcium absorption ↑	Gut urease ↓
Feed intake ↑	Plasma nutrients ↑	
	Gut energy loss ↓	

Source: Ewing and Cole [29]

Exogenous enzymes are widely used in cattle diets under a wide range of feeding strategies. They improve nutrient digestibility and consistency of feces in cattle. For instance, exogenous amylase improves the digestibility of dietary starch both in ruminants and non-ruminants [27].

According to Chow and Russell [25], a wide range of substances considered feed additives that may be classified as technological, organoleptic, nutritional and zoo technical (i.e. increasing animal production or performance).

In spite of the different emphasis of the mode of action of the rumen and gut-active feed additive growth promoters, their effects on the efficiency of performance is very similar with a 6 to 8% improvement in Feed conversion efficiency [28]. Some of physiological, nutritional and metabolic effects of feed additive growth promoter are presented in Table 2.

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 [30]. 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 [1].

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) [31].

Estradiol has estrogenic action (i.e. responsible for female characteristics); testosterone has androgenic action (i.e. responsible for male characteristics); and progesterone has gestagenic action (i.e. 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 [32].

Estradiol promoted growth by stimulating appetite and improving FCE [31]. 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 [33]. 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 tissues in the body to improve growth rate of animal [34]. Trenbolone acetate (TBA) is a synthetic steroid with an anabolic potency that may exceed that of testosterone. It is a pro-drug that converts into its active form 17β- trenbolone, which isomerizes into 17α-trenbolone. 17β-trenbolone is the major form occurring in muscle tissue, whereas the 17α-epimer is the major metabolite occurring in liver and in the excreta including bile. It is assumed to exert its anabolic action via interaction with androgen and glucocorticoid receptors [35].

Zeranol is derived from the naturally occurring myco-estrogen-zearalenone and is a potent estrogen receptor agonist *in vivo* and *in vitro* [36]. Its actions resemble those of estradiol [37] and used alone or in combination with TBA as a hormonal growth promoter in various products [38].

Growth Hormones: Growth hormone (GH) or somatotropin (ST) is a single polypeptide chain consisting of 191 amino acids, varying considerably between species [12]. It increases weight gain by stimulates metabolism and protein accretion concurrent with a reduction in fat deposition [21].

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% [39]. Though the use of BST is primarily concentrated on increasing milk production, 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 β-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 β1 and β2 receptors, leading to increased muscle protein synthesis [14, 26]. In muscle tissue, β-agonists promote protein synthesis and cell hypertrophy by inhibition of proteolysis. In adipose tissue, β-agonists promote lipolysis [40]. They may have a secondary mechanisms mediated by other hormones by increasing blood flow [41].

A wide range of compounds has been investigated as β-agonists including cimaterol, clenbuterol, fenoterol, isoprenaline, mabuterol, ractopamine, salbutamol, terbutaline and zilpaterol. Zilpaterol, present as an active β2-agonist in Zilmax®, is one of the new β-agonists officially registered for fattening purposes in cattle in Mexico and South Africa. Zilpaterol hydrochloride is a powerful β-agonist, which is more effective than ractopamine, but only about one-tenth effective as clenbuterol [42].

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) [39].

When β-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 [43] and a ‘rebound’ when the product is removed, leading to an increase in fat deposition and a reduction in muscle mass [35]. The most effective use of a repartitioning agent is therefore in the finishing period in the one to two months prior to slaughter.

Probiotics: Probiotics are mono or mixed culture of living microorganisms, which induce beneficial effect on the host by improving the properties of the indigenous micro- flora [44]. Several microorganisms have been considered as probiotics including fungi particularly mushroom and yeast, bacteria and mixed cultures comprising of various microbes [45]. Bacteria are more commonly reported as probiotic than fungi. The microorganisms used as probiotics are indicated in Table 3.

Genera *Lactobacillus* [46] and *Bifidobacteria* [47] are the mostly reported. Other bacteria that have been used, though to a lesser extent in poultry and animal probiotics include *Bacillus*, *Enterococcus*, *Streptococcus*, *Lactococcus*, *Pediococcus* and *Selenomona scerevisiae* [39].

Table 3: Microorganisms used as probiotics

Genus	Bacterial species
Lactobacillus	*L. acidophilus, L. casesi, L. rhamnosus, L. reuteri, L. plantarum, L. fermentum, L. brevis L. helveticus and L. delbruckei.*
Lactococcus	*L. lactis*
Enterococcus	*E. faecium*
Streptococcus	*S. thermophiles*
Pediococcus	*P. pentosaceus*
Bacillus	*B. subtilis, B. cereus, B. toyoi B. natto, B. mesentericus and B. lechentericus*
Bifidobacterium	*B. bifidum*
	B. pseudolongum
	B. breve
	B. thermophilum
Saccharomyces	*S. cerevisiae*
A virulent Escherichia coli	*E. coli*

Source: Ouwehand *et al*. [48] and Lodemann *et al*. [49]

Probiotics are commonly administered to animals orally either through the feed or drinking water. Recently, the use of the lactate-utilizing bacterium *Megasphaera elsdenii* as a probiotic has yielded interesting results in acidosis prevention and performance enhancement. Drenching *Megasphaera elsdenii* intra-ruminally has been effective in increasing rumen pH and decreasing lactate concentrations during a rapid transition from forage to a high concentrate diet [50]. In terms of acidosis prevention and enhancement of growth performance, the inclusion of probiotics in beef cattle diets is perhaps the second most adopted practice after ionophores [51].

Interestingly, a link between rumen abundance of *Megasphaera elsdenii* and milk fat depression has been recently identified [52] which can be extremely important in the future development of probiotics with application in dairy diets. The main limitation to using *Megasphaera elsdenii* as a probiotic is the fact that strict anaerobiosis is required to maintain a viable culture [53].

The mode of action of probiotics includes; competitive exclusion of pathogenic bacteria (Such as *E. coli* and *Salmonella* species), [1, 54] immune modulation [55], producing antibiotic substances, decreased intestinal pH [14], stimulating synthesis of vitamin B-groups, providing digestive enzymes and increasing of production of volatile fatty acids [14, 56].

For instance, *Lactobacillus* species which is found in many probiotic products produces antimicrobial lactic acid and bacteriocins (Antibacterial peptides) such as nisin, lactobrevin, acidophilin, acidolin, lactobacillin, lactocidin and lactolin [57]. Effects of Probiotics depends on the combination of selected bacterial genera, their doses and on the interactions of probiotics with some pharmaceuticals, feed composition, storage conditions and feed technology [58], they can also regulate anti and pro-inflammatory cytokine production [59] and natural killer cells [60].

Importance of Growth Promoters in Cattle Production: Cattle producers use growth promoters to increase growth rates and improve overall efficiency and product quality of cattle. Growth promoters are used widely in both the grazing (Grass fed) industry and the intensive feedlot industry of cattle [61]. In grass fed beef systems, the economic benefits from using growth promoters can come from higher growth rates per day, animals can be sold at heavier weights at the same age, animals can be sold earlier at similar weights, higher prices if better growth rates result in premium markets. Earlier sale of non-breeding cattle allows more breeders to be run on the same area. In feedlots, benefit of growth promoters is mainly from a higher feed conversion efficiency and greater throughput as animals reach the target weight more quickly [62].

Public Health Impact of Growth Promoter: 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. A drug that illustrates both potential problems is chloramphenicol.

Gassner and Wuethrich [63] had demonstrated the presence of chloramphenicol metabolites in meat products and linked the presence of these antibiotic residues in meat with the occurrence of aplastic anaemia in humans cannot be ruled out.

Antibiotics are illegally used for growth promotion in food animal production in many countries. These conditions favor the selection and spread of antibiotic resistant bacteria among animals, to the environment and eventually to humans, where they cause infections that are more difficult to treat, last longer or are more severe than antibiotic sensitive infections [64].

Food animals are an important reservoir of non-typhoidal *Salmonella*, as well as *Campylobacter* and some types of *E. coli* infections of humans [65]. Recent research suggests that food animals (Particularly pigs) may also be a reservoir of some strains of methicillin resistant *Staphylococcus aureus*(MRSA) for humans, although it appears that people are the major reservoir for most epidemiologically important strains of MRSA [66]. While the major public health impact from food animals is normally attributed to food borne *Salmonella* and *Campylobacter*, recent research is making it increasingly apparent that food animals are also an important reservoir of antibiotic resistant *E. coli* urinary tract and probably blood stream infections of humans [67].

Hormonal residues can adversely affect the immune system and can leads to an increase in certain common cancers. It also affects many aspects of human development and reproduction. The only evidence of such an effect comes from high levels of hormones injected into experimental animals. According to evaluations by the International Agency for Research on Cancer (IARC), there is currently sufficient evidence for the carcinogenicity of estradiol and limited evidence for the carcinogenicity of testosterone to humans. Experiments with some of the other compounds used in implants have shown that, under certain conditions, they may cause adverse effects in experimental animals [65].

Progesterone increases the incidence of ovarian, uterine and mammary tumors in laboratory animal experiments [68].

Zeranol stimulates estrogen receptors dependent cell proliferation in mammary glands which results in human breast cancer [37]. Although some recent data indicated that estradiol- 17β has genotoxic potential, Joint Expert Committee on Food Additive scientists pointed out that there are no data demonstrating that concentrations below the no-hormonal-effect level cause adverse effects in animals or humans [69]. Some carcass traits can be changed by the use of implants, with lower dressing percentages reduced marbling and a reduction in top grade carcasses being reported [70].

The use of beta agonists, such as ractopamine more effective for cattle production, but consumption of animal products that contain ractopamine residue have increase the toxicological risk on human health and also causes cardiovascular disease [71].

Probiotic producers, medical professionals and public health officers consider some form of system to monitor the health outcomes of long-term probiotic administration. Characterization of each strain of microorganism that used in production of probiotics must be on bases of guideline established by a working group conveyed of jointly by the FAO and WHO, in which they considered the safety probiotic products on human health. Improper usage of the probiotic production guideline results in developments of pathogenic microorganisms for both human and animal health [72].

The FDA, WHO, American dietetic association and national institutes of health have independently stated that dairy products and meat from Bovine somatotropin (BST) treated cow are safe for human consumption. The American cancer society issued a report declaring “the evidence for potential harm to human, from Bovine somatotropin (BST) milk, is inconclusive [73].

Policies on Growth Promoters: The World Health Organization [65] published a report on the medical impact of the use of antimicrobials in food animals suggesting a link between the two on an epidemiological basis. This report [74] recommends, on precautionary grounds, that national governments adopt a proactive approach to reduce the need for antimicrobial use in animals and establish surveillance of antimicrobial usage and resistance. With respect to the use of antimicrobial growth promoters, WHO suggests that use of antimicrobial growth promoters that are in classes also used in humans be terminated or rapidly phased out, by legislation if necessary, unless and until risk assessments are carried out.

On a global level, a recent joint workshop was held involving the WHO, Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE) on nonhuman antimicrobial usage and antimicrobial resistance. The resulting report recommends implementation of the WHO global principles for the containment of antimicrobial resistance in animals intended for food [69].These principles include the withdrawal from food animal production of AGP that are in classes also used to treat human disease unless and until a risk assessment is carried out [74].In addition, the report recommends the implementation on a national level of risk assessment studies and establishment of surveillance programs to monitor antimicrobial growth promoter use and antimicrobial resistance in bacteria from food animals.

Denmark was among the first countries to ban the use of hormones for growth promotion in meat animals, banning them in 1963. Concern about growth-promoting hormones became widespread in Europe in 1977 after the discovery that a number of young boys in Italy had begun to develop breast cancer.

Researchers suggested that estrogen in poultry or meat might have been related to the incident [38].

Whereas the EU has banned the use of all hormones, other countries do allow the use of steroid hormones and hormone-like substances in various combinations with the aim to improve weight gain and feed efficiency in livestock farming. Recommended application occurs in the form of small implants or devices, containing the active hormones, into the subcutaneous tissue of the ears. Both ears are completely discharged at slaughter [68].

In the United States, Canada, Australia, New Zealand and in some countries in South America, Asia and Africa the natural hormones - testosterone, 17ß-oestradiol and progesterone - and the synthetic hormones trenbolone, zeranol and melengestrol acetate can be used to promote growth [75].

Currently, five hormones (Progesterone, testosterone, estradiol-17β, zeranol and trenbolone acetate) are approved for implants in cattle in the U.S.A. But these implants have been officially prohibited in Europe since 1989.

Hormone implants are widely used in the U.S.A., Australia and Canada. According to a review by Brumby [40] approximately 30 countries have approved one or more of these implants for enhancing the growth of cattle. Use of these implants in cattle according to recommended procedures was declared safety by the; FDA, which approved 11 formulations of implants between 1956 and 1996, EEC Scientific Working Group on Anabolic Agents, chaired by Dr. G.E. Lamming in 1987 and FAO/WHO Joint Expert Committee on Food Additives [73].

The focus of bans in Sweden has been on antibiotics for growth promotion, rather than hormones. In 1986 Sweden banned all use of antibiotics for the purposes of growth promotion. Sweden was among the first countries to implement the recommendations of the United Kingdom's 1969 Swann Commission, which recommended restricting the use of antibiotics and prohibiting specific drugs in animal feed. In particular, the Swann Committee cautioned that antibiotics used for therapy should not be given to food animals [10].

Denmark introduced its first antibiotic ban in May 1995 when it banned the use of avoparcin in the country. This followed the release of a 1993 report that linked the emergence of the antibiotic-resistant bacteria, such as vancomycin-resistant *Enterococcus faecium* (VREF) to the administration of avoparcin as a growth promoter in food animals [76]. Subsequent findings in Germany and Denmark confirmed the relationship between VREF and the use of avoparcin. In spite of the 1995 avoparcin ban, the total use of antimicrobials for growth promotion continued to increase until January 1998 when Denmark banned a second growth promoter, virginiamycine [77].

Following the actions in European countries such as Sweden and Denmark, the Commission of the European Union banned the use of avoparcin as a growth promoter in all EU member states in 1997 [78]. In the EU, feed additives cannot be placed on the market unless they are authorized based on scientific evaluation of their efficacy, effect on animal and human health and on the environment [18].

There are currently no β-agonists registered in the EU for use in cattle as growth promoters, indeed in the EU this class of compound is specifically prohibited under EU Directive 96/22/EC.There is one product registered as a growth promoter in cattle in South Africa and Mexico zilpaterol (Zilmax, Hoechst Roussel Vet) – and one in pigs in the USA, Mexico, Brazil, Philippines and Korea – ractopamine [79].

This prohibition prompted an international trade dispute, with Canada and the United States contesting the ban. In 1997 a World Trade Organization (WTO) panel ruled that the EU prohibition was not consistent with the agreement on the application of Sanitary and Phyto-sanitary Measures. On appeal by the EU, the WTO appellate body reversed most of the initial panel's decision, but upheld the finding that the prohibition did not comply with the requirement in the agreement that measures should be based on a relevant assessment of the risks to human health [75].

CONCLUSION

Different types of growth promoters (GP) used in cattle are feed additives, anabolic implants, growth hormones, β-agonists and probiotics. They have different mechanism of action, but their last effect is improvement of cattle production by increasing the feed conversion efficiency, average daily gain and carcass quality or milk production of animals. Though growth promoters have importance for cattle production, the final consumer can be affected by different adverse effects like antibiotic drug resistance, carcinogenic effects and potential pathogen. For this reason, antimicrobial growth promoters that are also used in humans and generally illegal use of a large variety of growth promoters should be terminated or controlled unless and until risk assessments are carried out. Countries should develop policy on the use of different animal growth promoters.

REFERENCES

1. Mader, T., 1997. Carryover and lifetime effects of growth promoting implants. Proc. OSU Symposium: Impact of implants on performance and carcass value of beef cattle. 88-94, Oklahoma Agric. Exp. Stn
2. Jensen, B., 2010. Alternative to Antibiotics as Growth Promoters. 5 M Enterprises Ltd, Benchmark House 3, Sheffield, England, pp: 1-3.
3. Herschler, C., W. Olmsted, J. Edwards, T. Montgornery and J. Sheldom, 1995. Production responses to various doses and ratio of estradiol benzoate and trenbolone acetate implants in steers and heifers. J. Anim. Sci., 73: 2873-2881.
4. Monseley, W., B. Paulissen, C. Goodwin and M. Clafin, 1992. Recombinant bovine somatotropin improves growth performance in finishing beef steers. J. Anim. Sci., 70: 421-425.
5. Delfino, J., W. Mathison and W. Smith, 1998. Effect of Basaloid on feedlot performance and energy partitioning in cattle. J. Anim. Sci., 66: 136-150.
6. Kirk, L., W. Greene, G. Schelling and F. Byes, 1995. Effects of monensin on Monovalents on metabolism and tissue concentration in lambs. J. Anim. Sci., 60: 1455-1490.
7. Kegley, B., R. Harvey and J. Spears, 1991. Effects of lysocellin and calcium level on mineral metabolism, performance, ruminal and plasma characteristics of beef steers. J. Anim. Sci., 69: 782-791.
8. Scarth, J., C. Akre and L. Van Ginkel, 2009. Presence and metabolism of endogenous androgenic-anabolic steroid hormones in meat producing animals. J. feed Addi. Expo. Risk Ass., 26(5): 640-671.
9. Allen, P. and W. Enright, 1999. Effects of administration of somatotropin on meat quality in ruminants. Arch. Fur. Gefl., 12: 201-219.
10. Wierup, M., 2001. The experience of reducing antibiotics used in animal production in the Nordic countries. Int. J. Anti. Agents, 18: 3.
11. Abd-Elhakeem, A., K. Abdel -Moty, F. El-Feel and M. Abu-Elawla, 1998. Reproductive performance of buffalo and Friesian calves as affected by flavomycine growth promoter. J. Anim. Prod, 35(1): 55-66.
12. Eversole, E., P. Fontenot and D. Kirk, 1996. Implanting trenbalone acetate and estrodiol in finishing beef steers. Nutr. Repo. Inter, 39: 995-998.
13. Allam, M., K. El-Shazly, B. Borhami and M. Mohamed, 2001. Effect of baker's yeast (Saccharomyces cerevisiae) supplementation on digestion in sheep and milk response in dairy cows. J. Nutrand Feeds, 4: 315-323.
14. Fuller, R., 1999. Probiotics for farm animals. J. Nutr. Rev., 8: 15-22.
15. Chen, G. and B. Russell, 1999. More monensin-sensitive, ammonia producing bacteria from the rumen. Appl. Env. Microb, 55: 1052-1055.
16. Newbold, J., R. Wallace and D. Walker, 1993. The effects of tetronasin and monensin on fermentation, microbial numbers and the development of ionophore-resistant bacteria in the rumen. J. Appl. Bact., 75: 129-34.
17. Corpet, D., 1998. The effect of bambermycin, carbadox, chlortetracycline and olaquindox on antibiotic resistance in intestinal coliforms. Clin. Infect Dis., 135(1): 329-339.
18. Gaines, A., L. Rollins and M. Selwyn, 1990. Effect of penicillin and virginiamycin on drug resistance in lactose-fermenting enteric flora. Anti-microbial Agents and Chemotherapy, 17: 428-433.
19. Mee, B., 1992. The selective capacity of pig feed additives and growth promotants for coliform resistance. J. Antibo. Agri, 4: 349-358.
20. Pressman, C., 1996. Biological applications of ionophores. Ann. Rev. Bio. Chem., 45: 501-530.
21. Richardson, F., A. Raun, E. Potter and P. Rathmacher, 1996. Effects of monensin on rumen fermentation in vitro and in vivo. J. Anim. Sci., 43: 657-669.
22. Nagaraja, T. and D. Titgemeyer, 2007. Ruminal acidosis in beef cattle: The current microbiological and nutritional outlook. J. Dairy Sci., 90 (l): 17-38.
23. Lowe, B., J. Ball, R. Carruthers, C. Dobos and C. Valemtine, 1991. Monensin controlled-release intra-ruminal capsule for control of bloat in pastured dairy cows. J. Austral. Vet., 68: 17-20.
24. Goodrich, R., E. Garrett, R. Gast, M. Kirick, D. Larson and C. Meiske, 1994. Influence of monensin on the performance of cattle. J. Anim. Sci., 58: 1484-1498.
25. Chow, M. and B. Russell, 1990. Effect of ionophores and pH on growth of Streptococcus bovisin batch and continuous culture. Appl. Env. Microb., 56: 1588-1561.
26. Mackinnon, J., 1997. The role of growth promoters in pig production. Vet. Soc., 17: 69-100.

27. Ankrah, N., L. Campbell, T. Tyler and R. Sokhansan, 1999. Hydrothermal and beta glucanase effects on the nutritional and physical properties of starch in normal and waxy hull-less barley. Anim. Feed Sci. Tech., 81: 205-219.
28. Lawrence, K., 1998. Growth promoters in swine. IN: Proceedings of the 15th IPVS Congress, Birmingham, England, pp: 337-343.
29. Ewing, W. and D. Cole, 1994. Bovine Medicine – Disease and Husbandry of cattle: Growth promoters in cattle. J. Liv. Gut, 12: 67-74.
30. Platter, J., D. Tatum, E. Belk, A. Scanga and C. Smith, 2003. Effects of repetitive use of hormonal implants on beef carcass quality, tenderness and consumer ratings of beef palatability. J. Anim. Sci., 81: 984-996.
31. Elmore, G., 1992. Focus on bovine reproductive disorders: managing cases of fetal mummification. Vet. Med., 87: 155-159.
32. Pepper, R. and H. Dobson, 2007. Preliminary results of treatment and endocrinology of chronic endo-metritis in the dairy cow. Vet. Repro, 120: 53-56,
33. Chang, C., A. Saltzman and A. Mizokami, 1995. Androgen Receptor in Eukaryotic Gene Expression. Int. J. Canc, 5: 1045-1049.
34. Wiebe, P., 2006. Progesterone metabolites in breast cancer. Endo. Rel. Canc, 13: 717-738.
35. Elliot, T., H. Crooks, D. Evoy, J. Gaughey and D. Kilpatrick, 1993. Observations on the effects of long-term withdrawal on carcass composition and residue concentrations in clenbuterol medicated cattle. Vet. Res., 132: 459-468.
36. Takemura, H., Y. Shim, K. Sayama, A. Tsubura, T. Zhu and K. Shimoi, 2007. Characterization of the estrogenic activities of zearalenone and zeranol in vivo and in vitro. J. Ster. Bio-chem. and Mol. Bio., 103(2): 170-177.
37. Leffers, H., M. Naesby, B. Vendelbo and M. Jorgensen, 2001. Oestrogenic potencies of zeranol, oestradiol, diethylstilboestrol, bisphenol-A and genistein. Implications for exposure assessment of potential endocrine disrupter Human Reproduction, 16: 1037-1045.
38. Yuri, T., R. Tsukamoto, N. Uehara, Y. Matsuoka and A. Tsubura, 2006. Biphasic effects of zeranol on the growth of estrogen receptor positive human breast carcinoma cells. Onc. Repor, 16(6): 1307-1312.
39. Lee, J., S. Knowles and G. Judson, 2010. Sheep Nutrition. 4th ed. CAB International: Wallingford, UK, pp: 285-312.
40. Brumby, P., 1999. The influence of growth hormone on growth in young cattle. J. Dairy Sci., 2: 683-689.
41. Mersmann, H., 1998. Overview of the effects of β-adrenergic agonists on animal growth including mechanisms of action. J. Anim. Sci. , 76: 160-172.
42. Anderson, D., V. Cracken, R.I. Aminov, M. Simpson and H. Gaskins, 2000. Gut microbiology and growth-promoting antibiotics in swine. J. Liv. and Feeds, 70: 101-108.
43. Re, G., P. Badino, A. Novelli and G. Girardi, 1994. Homologous β-adreno-receptor down regulation and heterologous estrogen and progesterone up regulation induced by repeated β2-adrenergic stimulation in the female reproductive tract of veal calves. IN: Proceedings of the 6th Congress of the European Association of Veterinary Pharmacology and Toxicology, Ed in Burgh, pp: 7-11.
44. Ghadban, G., 2002. Probiotics in broiler production. Arch. Fur. Gefl., 66: 49-58.
45. Willis, L., S. Isikhuemhen and I. Ohimain, 2011. Effect of phase feeding of fungus Myceliated grain on oocyst excretion and performance of boiler chicken. Int. J. Poult. Sci., 10(1): 1-3.
46. Taheri, R., H. Moravej, F. Tabandeh, R. Zaghari and M. Shivazad, 2009. Screening of lactic acid bacteria toward their selection as a source of chicken probiotic. Poult. Sci., 88: 1586-1593.
47. Patterson, A. and M. Burkholder, 2003. Application of prebiotics and probiotics in poultry production. J. Poult. Sci., 82: 627-631.
48. Ouwehand, C., S. Salminen and E. Cisolauri, 2002. An overview on beneficial effects of Probiotics. J. Anim. Nutr, 82: 279-289.
49. Lodemann, U., M. Lorenz, D. Weyrauch and H. Martens, 2008. Effects of Bacillus cereus var. toyoias probiotic feed supplement on intestinal transport and barrier function in piglets. Arch. Anim. Nutr, 62: 87-106.
50. Henning, P., C. Horn, D. Steyn and H. Meissner, 2010. The potential of Megasphaera elsdenii isolates to control ruminal acidosis. Anim. Feed Sci. Technol., 157: 13-19.
51. Beauchemin, A., W. Yang, D. Morgavi and Z. Leedle, 2003. Effects of bacterial direct feed microbial and yeast on site and extent of digestion. J. Anim. Sci., 81: 1628-1640.

52. Palmonari, A., M. Stevenson, D. Mertens and P. Weimer, 2010. pH dynamics and bacterial community composition in the rumen of lactating dairy cows. J. Dairy Sci., 93: 279-287.
53. Bomba, A., R. Nemcova, B. Gancarcikova and D. Mudronovam, 2002. Improvement of the probiotic effect of microorganisms by their combination with maltodextrins, fructo-oligo sacharides and polyunsaturated acids. Appl. Env. Microb., 88: 95-99.
54. Mountzouris, C., H. Beneas, P. Tsirtsikos, H. Kalamara and K. Fegeros, 2006. Efficacy of a new multi-strain probiotic product in promoting broiler performance and modulating the composition and activities of cecal microflora. International Poultry Science Forum. Atlanta, Georgia.
55. Lan, Y., M. Verstegen, S. Taminga and B. Williams, 2005. The role of the commensal gut microbial community in broiler chickens. J. Poult. Sci., 61: 95-104.
56. Rolfe, E., 2000. The role of probiotic cultures in the control of gastro-intestinal health. J. Nutr. Anim. Sci., 130: 396-402.
57. Maxwell, F., S. Duncan, G. Hold and S. Stewart, 2004. Isolation, growth and prebiotics and probiotic potential of novel Bifido bacteria from pigs. J. Bifid. Anaerob, 10: 33-39.
58. Chen, Y., S. Kwon and H. Kim, 2005. The effects of dietary Biotite V supplementation as an alternative substance to antibiotics in growing pigs. Anim. Sci., 18: 1642-1645.
59. Roselli, M., A. Finamore, M. Britti, P. Bosi, I. Oswald and E. Mengheri, 2005. Alternatives to in-feed antibiotics in pigs. J. Prob. Feeds, 54: 203-218.
60. Matsuzaki, T. and J. Chin, 2002. Modulating immune responses with probiotic bacteria. Immun. Cell Bio., 78: 67-73.
61. Jin, L. and X. Zhao, 2000. Intestinal receptors for adhesive fimbriae of enetro toxigenic Escherichia coli (ETEC) K88 in swine. Appl. Microb. and Biotech, 54: 311-318.
62. Park, Y., H. Namkung and K. Paik, 2001. Effects of supplementary enzymes or probiotics on the performance and ammonia gas production in weanling pigs. J. Anim. Sci., 43: 485-496.
63. Gassner, B. and A. Wuethrich, 1994. Pharmacokinetic and toxicological aspects of the medication of beef-type calves with an oral formulation of chloramphenicol palmitate. J. Vet. Pharm. and Therap, 17: 279-283.
64. Barza, B., 2002. Potential mechanisms of increased disease in humans from anti-microbial resistance in food animals. J. Anim. Physio. and Nutr, 34(3): 123-125.
65. WHO, 1997. The medical impact of the use of antimicrobials in food animals: Report of a WHO meeting, Berlin, Germany.
66. Weese, S.and D. Evans, 2010. Methicillin-resistant Staphylococcus auras and Staphylococcus pseudintermedius in veterinary medicine. Vet. Micro, 140(4): 418-429.
67. Manges, H., 2007. Retail meat consumption and the acquisition of antimicrobial resistant Escherichia coli causing urinary tract infections. Food borne Pathogen Dis., 4(4): 419-431.
68. Galbraith, H., 2002. Hormones in international meat production. Biological, Sociological and Consumer Issues, 15: 243-314.
69. WHO, 2004. Proceedings of the Joint FAO/OIE/WHO expert workshop on non-human antimicrobial usage and antimicrobial resistance: Scientific assessment. WHO/CDS/DIP/ZFK/04.20, Geneva, Switzerland, pp: 1-71.
70. Kuhl, G., D. Simms and P. Hartman, 1999. Sequential implanting with Synovex-S or Synovex-S + Finaplix-S on steer performance and carcass characteristics. J. Anim. Sci., 67(1): 434.
71. Testa, C., G. Boatto and A. Pulina, 2000. Evaluation of conventional screening procedures for the detection of new beta-agonists. J. Stero. Biochem, 13(11): 1337-1345.
72. Krehbiel, R., S. Rust, G. Zhang and E. Gilliland, 2003. Bacterial direct-fed microbials in ruminant diets and its Performance response and mode of action. J. Anim. Sci., 81(2): 120-132.
73. Joint FAO/WHO, 1999. Expert Committee on Food Additives. Summary and Conclusions of the Fifty Second Meeting, Rome.
74. WHO, 2000. Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food. WHO/CDS/CSR/ APH/2004., Geneva, Switzerland, pp: 1-23.
75. Hayes, D., 2002. Technology choice and the economic effects of a ban on the use of antimicrobial feed additives in swine rations. Rec. Adv. Anim. Nutr, 32: 231-239.
76. Bates, J., Z. Jordens and B. Selkon, 1993. Evidence for animal origin vancomycine resistant enterococci. J. Anim. Sci., 42: 490-491.

77. Hammeroun, A., 2007. Danish Integrated Antimicrobial Resistance Monitoring and Research Program. J. Appl. Bact, 14: 132-136.
78. European commission directive, 1997. Amending Council Directive concerning about additives in feeding stuffs. Official Journal of the European Communities, 97: 3511-3513.
79. Marchant Forde, N., C. Lay and A. Schinckel, 2003. The effects of ractopamine on behavior and physiology of finishing pigs. J. Anim. Sci., 81: 416-422.