Review on Growth Hormone in Animals

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Summary
Hormones are chemicals produced by animals to co-ordinate their physiological activities. Steroid hormones fulfill an important role at different stages of mammalian development comprising prenatal development, growth, reproduction and social behavior. One hormone can have multiple actions; example the male hormone testosterone controls many processes from the development of the foetus, to libido in the adult. Hormones produced by the bodies of humans and animals are called endogenous or natural hormones. Compounds chemically synthesised to mimic the effect of natural hormones are called synthetic or xenobiotic hormones. Hormones are vital in normal development, maturation and physiological functioning of many vital organs and processes in the body. However, like any other chemicals of natural or synthetic origin, hormones may be toxic to living organisms under certain circumstances. The toxicity may be due to an excess of its normal physiological action. This may be the result of excessive exposure to the substance. Bovine somatotropin, also known as bovine growth hormone, is a protein hormone produced by the pituitary gland of bovines. Growth hormone and Prolactin are polypeptide hormones, which have evolved from a common ancestral gene. Estrogen is the main hormone affecting growth, development, maturation and functioning of reproductive tract as well as the sexual differentiation and the behavior. Finally growth hormones must be used properly in relation to their dose, site of administration and implantation by professionals was recommended.
Keywords: *Bovine Growth Hormone, Implantation, Natural Growth Hormone,*

1. Introduction

Livestock farming has undergone a significant transformation in the past few decades. Production has shifted from smaller, family-owned farms to large farms that often have corporate contracts. Most meat and dairy products now are produced on large farms with single species buildings or open-air pens. Modern farms have also become much more efficient. Since 1960, milk production has doubled, meat production has tripled, and egg production has quadrupled. Improvements to animal breeding, mechanical innovations, and the introduction of specially formulated feeds and animal pharmaceuticals have all increased the efficiency and productivity of animal agriculture. It also takes much less time to raise a fully grown animal (Hribar, 2010).

It is known that the productivity of livestock and other farming characteristics, such as meat yield, growth rate, milk production, milk composition, and other are inherited from generation to generation, and their formation and functional characteristics are determined by genes. Currently, with the help of new molecular methods, genetic evaluation of cattle is carried out directly analysing the DNA, which contains all the genetic information of animal's inherited characteristics. These methods allow for detailed investigation of bovine genome, and determination as which genes and how operate and influence meat and milk quantity and quality, what genetic factors influence cattle health, genetic diversity and genetic relationships among breeds (Krasnopiorova *et al.,* 2012).

Hormones are chemicals produced by animals to co-ordinate their physiological activities. They act as messengers, produced in and released from one kind of tissue to gradually stimulate or inhibit some process in a different tissue over a long period. Steroid hormones fulfill an important role at different stages of mammalian development comprising prenatal development, growth, reproduction and sexual and social behavior. The importance of individual hormones varies between sexes and age and a disruption of the endocrine equilibrium may result in multiple biological effects (Passantino, 2001).

Hormones are vital in normal development, maturation and physiological functioning of many vital organs and processes in the body. However, like any other chemicals of natural or synthetic origin, Hormones may be toxic to living organisms under certain circumstances. The toxicity may be due to an excess of its normal physiological action. This may be the result of excessive exposure to the Substance, following absorption of a large dose, or because the physicochemical nature of the substance gives it greater (more 'potent') or more prolonged activity of the same type, or because the hormonal action (endocrine effect) occurs at an abnormal time during development or Adult life, or is an action on an organism of the in appropriate sex. Hormones, like other chemicals, May also exert direct toxic actions not related to their endocrine physiological effects (Bolt *et al*., 2001).

Growth hormone (GH) and Prolactin (PRL) are polypeptide hormones, which have evolved from a common ancestor. Although PRL and GH are produced by cells of the anterior pituitary that have a common stem cell, there are clear and distinct functions 43 of these two hormones. Both hormones have been shown to be important for control of mammary growth, lactogenesis and lactation (Bole-Feusot *et al*., 1998).

Bovine somatotropin, also known as bovine growth hormone or BGH, is a protein hormone produced by the pituitary gland of cows. There are 20 amino acids that comprise the structure of all proteins and each specific protein has a unique sequence of amino acids similar to the use of letters in the alphabet to spell a word. The sequence of the protein bST is 191 amino acids. Recombinant-DNA technology has allowed for the commercial production of rbST which is biologically equivalent to natural pituitary-derived bST and has the same amino acid sequence plus one extra amino acid (the essential amino acid methionine) at one end (Bauman and Collier, 2010).

Therefore, the objectives of this seminar are:

- To give an overview of the types, uses, methods and site of administration of growth hormones.
- To highlight their impact on animals and human beings as well as on the environment.
- To show the economic importance of growth hormones in veterinary and animal science practices.

2. Growth hormone

2.1. Growth hormones and their types

Hormones function in four broad areas: reproduction; growth and development; maintenance of the internal environment; and production, utilization and storage of energy. One hormone can have multiple actions. For example, the male hormone testosterone controls many processes from the development of the fetus to libido in the adult. One function may be controlled by multiple hormones: the menstrual cycle involves oestradiol, progesterone, follicle-stimulating hormone and luteinizing hormone (Josling *et al.,* 1996).

Growth hormone makes 8.8% muscle mass increase without increased exercise, 14.4% decrease in fat without Change in diet or habit, enhanced sexual performance, increased cardiac output, better kidney function, faster wound healing, hair re-growth, mood elevation, improve sleep, enhances activities of all other hormones, improves diet, regeneration in growth of heart, liver, kidney, increase in immune functions, increase in exercise performance, decrease in blood pressure, develops stronger bones, younger and thicker skin, removes wrinkles, increase memory retention and decrease in hot flashes for women (Kopchick, 2004).

Throughout history, a large number of natural and synthetic substances have been applied in stock farming to speed up and improve animal growth, and to decrease feed costs. Anabolic agents or growth promoters are metabolic modifiers which improve efficiency and profitability of livestock production and improve carcass composition (Dikeman, 2007). Main physiologic effects of anabolic steroids include growth of muscle mass and strength, increase bone density, increasing of sex organs particularly important in the fetus and at the puberty the appearance of secondary sexual characteristics. The group of anabolic growth promotants includes compounds that naturally occur in an animal's body and synthetic chemicals that mimic the action of naturally occurring compounds (Cavalieri *et al*., 2005).

2.1.1. Natural hormones

Hormones (chemicals) produced by the bodies of humans and animals are called endogenous or natural hormones. Natural hormones are secreted into the blood stream by specialized cells and travel throughout the body. Hormones act by binding protein receptors present in hormone-responsive tissues. The receptor undergoes a conformational change, binds to specific DNA sequences and regulates specific genes within a cell. There are naturally occurring hormones produced by humans and animals: oestradiol-17b, progesterone and testosterone (hereafter also referred to as natural hormones) (Josling *et al*., 1996).

Oestradiol-17B is a sex steroidal hormone with oestrogenic action (i.e., responsible for female characteristics); testosterone is a sex steroidal hormone with androgenic action (i.e., responsible for male characteristics); progesterone is a sex steroidal hormone with gestagenic action (i.e., responsible for maintaining pregnancy). These three hormones are produced throughout the lifetime of each individual and are required for normal physiological functioning and maturation. Hormone levels vary with the tissue, with the species of animal and with the sex and individual. Hormone levels vary most dramatically with puberty, pregnancy and castration (Josling *et al.,* 1996).

2.1.2. Synthetic hormones

Synthetic hormones are xenobiotic substances that do not naturally occur in animal organisms. These exogenous drugs mimic the effects of natural endogenous hormones, such as the case of synthetic versions of estradiol, progesterone and testosterone: zeranol, melengestrol acetate (MGA) and trenbolone acetate, respectively. In general and due to their entirely exogenous character, since these compounds do not exist naturally, there are no major difficulties in determining analytic synthetic steroids. Thus, their mere presence in the animal organism is a clear evidence their administration (Regal *et al*., 2008).

The following natural hormones and their synthetic alternatives have been approved by the Veterinary Drugs Directorate (VDD) for use in Canadian beef production.

Table 1: Natural hormones and their synthetic alternatives

Natural Hormones	Synthetic Hormones
Estradiol (estrogen)	Zeranol
Progesterone	Melengestrol acetate
Testosterone	Trenbolone acetate

Source: Canadian Animal Health Institute (CAHI, 2000).

2.2. Growth hormones and site of administration

Hormones are used as growth promoters in livestock production. Producers who treat their animals with hormones at the same time feed them high energy, nutrient rich grains in balanced diets. Hormones also help the animals improve its nutrient absorption. Improved nutrient absorption equates to less need for feed in order for the animal to reach its finish weight (market weight). In addition, hormone helps to improve meat quality by changing the deposition of fat producing the lean meat that consumer desire. So essentially, the animal grows larger, faster, without becoming excessively fat. Growth hormones are administered to cattle through an implant in the ear, a part of the animal that is not used for human consumption (CAHI, 2000).
(See figure 1 bellow).

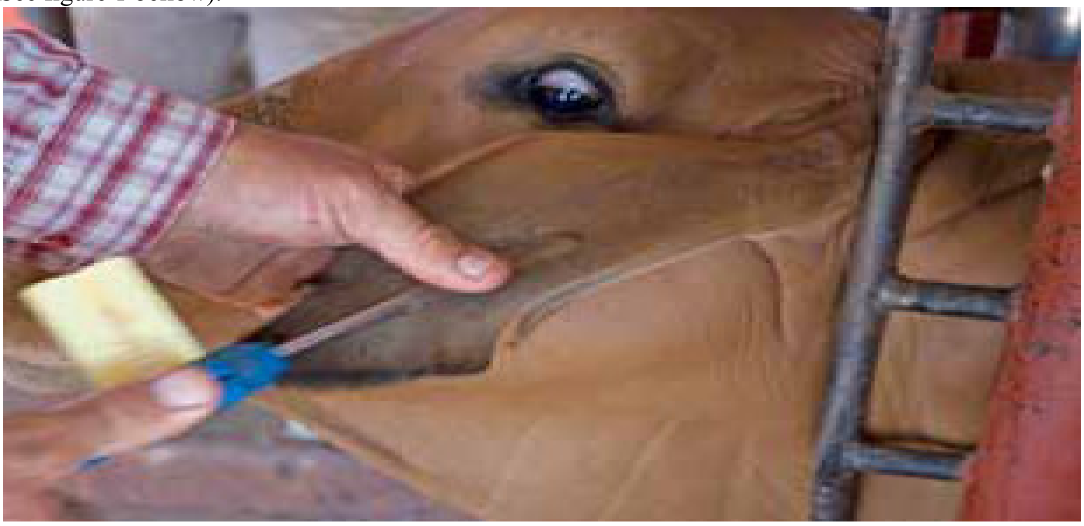

Figure 1: Implantation site of growth hormones on the ear.
Source: (Newton, 1996)

America's cattle producers use growth hormones to safely produce more of the lean beef that consumers demand while using fewer resources, like land and feed. Sometimes referred to as Cattle growth hormones or steroids.These production technologies have been used for nearly 60 years to help cattle efficiently convert their feed into more lean muscle. Growth hormones typically are administered through a small pellet (called an implant) that is placed under the skin on the back of an animal's ear, but some can be administered through the animal's feed (Newton, 1996).

The hormones in growth promoting implants include estrogens (Estradiol and Zeranol), androgens (testosterone and trenbolone acetate or TBA) and progestins (progesterone and melengestrol acetate or MGA) (CBBNCBA, 2007).

Hormone implants containing Estradiol benzoate / progesterone were first approved in 1956 by the U.S. Food and Drug Administration (FDA) for increasing growth, feed efficiency, and carcass leanness of cattle. Later, other implants containing testosterone, Zeranol, trenbolone acetate, and combinations of these hormones were developed and approved for use in cattle by the FDA. Currently, five hormones (progesterone, testosterone, estradiol-17β, zeranol, and trenbolone acetate) are approved for implants in cattle in the U.S.A. (Doyle, 2000).

Growth promotants are primarily given to cattle in the form of small pellets placed under the skin in the animal's ear. These ear implants dissolve slowly over a 100-120 day period. The ear is used because ears do not enter the food supply. Implants work by changing what happens to the nutrients that cattle eat. Muscle growth is enhanced at the expense of fat deposition. Because muscle is more efficient for the animal to produce compared to fat, the animal grows faster with less feed consumed (Loy, 2011).

2.3. Applications of growth hormones in agriculture

Many of the diverse actions of GH, including stimulation of linear growth, anabolic and lipolytic activity, enhancement of lactation, stimulation of immune function, and effects on bone mineralization, are potentially beneficial in agricultural animal uses. Cloning of the GH genes and the ability to produce virtually unlimited quantities of biologically active GH by recombinant technology created opportunity for practical use of this material. Recombinant bovine GH is currently marketed in the United States for the purpose of increasing milk production in dairy cattle, and there is considerable evidence that GH treatment can markedly improve milk yield in cattle, sheep, and goats. Implanting hormonal growth promoters 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 production (Mader, 1997; Platter *et al.,* 2003).

Oestradiol 17-B is the most active of the female sex hormones synthesized and secreted mainly by the ovary, the adrenals and the testis. Oestradiol is synthesized and secreted in early stages of embryogenesis and has an active role in the normal development of the female sex accessories during the lifetime of females. It has been used to induce parturition (birth) especially in sheep, a species in which an associated oestradiol-induced increase in mothering ability has also been recorded (Poindron, 2005).

2.4. Metabolism and mechanism of action

Growth hormone acts on liver, kidney, fibroblast, and thymus epithelial cells. In the liver, GH causes the gene expression and production of insulin-like growth factor-1 (IGF-1, somatomedin C), and IGF-1 enhances the growth through causing proliferation of cartilage cells, biosynthesis of chondroitin sulfate, hyperplasia and proliferation of various tissue cells, and protein anabolism, and enhances secretion of thymulin from thymus cells (Casanueva, 1992)

Metabolic effect of GH is biphasic. Administration of GH tentatively shows insulin-like effect (suppression of amino acid decomposition, enhancement of protein synthesis, decrease of blood glucose, amino acids and free fatty acids), but later it causes increase of free fatty acids owing to degradation of fat in adipose tissue, raising blood glucose, and shows insulin antagonistic actions such as suppression of glycolysis, glycogen content increase in muscle, and lowering insulin sensitivity in peripheral tissue. GH has also prolactin like actions such as retention of Na, K, Mg, Ca, and P, enhancement of Ca absorption in small intestine, development of mammary gland, enhancement of milk secretion (Strobl and Thomas, 1994)

Growth hormone, which is synthesized in and released from the somatotroph cells of the anterior pituitary gland, is involved in a variety of biological processes. These processes include longitudinal bone growth, skeletal muscle growth, lipolysis, the inhibition of lipogenesis, lactation and reproduction. Perhaps most significantly, GH stimulates liver IGF-I synthesis. The synthesis and secretion of GH are under the control of GH releasing hormone (stimulatory) and somatostatin (inhibitory) from the hypothalamus. Growth hormone is stored in secretory granules within the somatotroph cells of the anterior pituitary gland and released into the circulation upon stimulation. In many species, including cattle, some of the GH in the circulatory system is bound to a GH binding protein. Despite being capable of competing with the GHR for GH binding, it is most likely responsible for enhancing GH action by increasing its half-life (Rhoads *et al*., 2010).

Most growth promotants are used to supplement existing hormones or compensate for missing hormones in an animal’s body. For example, steers (castrated bulls) implanted with a growth promotant gain weight at about the same rate as a bull. The hormones in growth promotants are metabolized or used by the animal’s body before it goes to harvest. Although these products vary in active ingredients and dose, they generally work by discouraging protein depletion and encouraging protein synthesis in cattle so they can gain leaner muscle from less feed (Cattlemen’s Beef Board and National Cattlemen’s Beef Association, 2007).

2.5. Effects of growth hormone in reproduction

Gonadal hormone secretion is under the control of chromosomal sex, which, in turn, controls the phenotype of non-gonadal tissue. The hormonal regulation of sexual differentiation of the mammalian reproductive system was established in the late 1940s by Jost. In his study, testes were removed from fetal male rabbits, inducing a female phenotype at birth. In contrast, transplantation of testis into female embryos induced a male phenotype. The early fetus has the potential to be either male or female and possesses not only an undifferentiated gonadal ridge, but also ‘precursors’ for both Mullerian and Wolfian ducts (Newbold and McLachlan, 1982). Growth Hormone (GH) is important factor in sexual maturation and attainment of puberty. External administration of GH has been shown to accelerate sexual maturation (Wilson *et al*., 1989)

Growth hormone is released in a pulsatile fashion that is particularly pronounced in males and is present in the plasma both in the free form and bound to GH binding protein (GHBP). Depending on the species, GHBP is derived from cleavage of the extracellular portion of the GH receptor (GH-R) or from alternative transcripts of the GHR/GHBP gene. Secretion of GH is controlled primarily by 2 hypothalamic factors: GH-releasing hormone GHRH) and somatostatin, which exert opposing influence on GH release (Giustina and Veldhuis, 1998).

Growth hormone, as its name suggests, is obligatory for growth and development. It is, however, also involved in the processes of sexual differentiation and pubertal maturation and it participates in gonadal steroidogenesis, gametogenesis and ovulation. It also has additional roles in pregnancy and lactation. These actions may reflect direct endocrine actions of pituitary GH or be mediated by its induction of hepatic or local IGF-I production. However, as GH is also produced in gonadal, placental and mammary tissues, it may act in paracrine or autocrine ways to regulate local processes that are strategically regulated by pituitary GH (Hull and Harvey, 1997).

Although the somatogenic and gonadotrophic axes have long been known to be closely linked during growth and sexual maturation, until recently the role of growth hormone (GH) in reproduction had been described as'more akin to fine tuning than that of a major player. Experimental studies suggest, however, that this statement underestimates the importance of GH in reproductive function, since GH modulates steroidogenesis, gametogenesis and gonadal differentiation as well as gonadotrophin secretion and responsiveness (Zachmann, 1992).

Mammary and placental roles for GH have also been proposed (Mol *et al.* 1996, Alsat *et al.,* 1997). Moreover, while these actions may reflect endocrine roles of pituitary GH, they may also reflect local autocrine or paracrine actions of GH produced in reproductive tissues. GH is usually, but not always, required for the timing of sexual maturation, since delayed or absent puberty is often associated with GH-deficient or GH-resistant states and GH administration accelerates puberty. For instance, in a cohort of 60 GH-deficient women, puberty occurred normally in only 16 and was delayed in 10 others. Puberty is similarly delayed in a large proportion of GH receptor (GHR)-knockout mice. GH may accelerate puberty by activating the luteinizing hormone (LH)-releasing hormone pulse generator and/or by potentiating androgen action (Bartke *et al*., 1999).

2.6. Factors regulating the activities of growth hormones

Growth Hormone (GH) is an anti-parallel four-helix bundle protein (Chantalat et al, 1995) secreted in a pulsatile manner by somatotrophs in the anterior pituitary gland (Edmondson et al, 2003). Its secretion is controlled by two neuropeptides namely Growth Hormone-Releasing Hormone (GHRH) and the Somatostatin. Somatostatin inhibits GH release without affecting GH synthesis. Several lines of evidence suggest that GHRH initiates GH pulses and somatostatin modulates the amplitude of GH pulses. Growth hormone also exerts a negative feedback effect on its own secretion. Daily subcutaneous administrations of GH for 2-5 days decrease the endogenous GH response to GHRH. This effect may be mediated through the secretion of IGF from the liver (Ross *et al*., 1987).

Estrogen is the main hormone affecting growth, development, maturation and functioning of reproductive tract as well as the sexual differentiation and the behavior. Growth hormone is also important factor in sexual maturation and attainment of puberty. Estrogen may possibility have a direct effect on growth hormone secretion via the binding to estrogen receptor-α due to its co-expression in growth hormone neurons in the medial preoptic area and arcuate nucleus. Estrogen may also have an indirect effect via the reducing insulin-like growth factor-1 feedback inhibition resulting with increased growth hormone secretion (David, 2013).

Estrogen is an intra ovarian factor affecting the function of hypothalamus, pituitary, liver, skeleton and calcium homeostasis (Turner *et al*., 1994). It is also a main reproductive hormone affecting growth, development, maturation and functioning of reproductive tract as well as the sexual differentiation and the behavior (Balthazart *et al*., 2009). Therefore exogenous estrogens have been used to increase the secretory characteristics of GH in several species including sheep (Misztal *et al*., 2007) and human (Weissberger *et al*., 1991).

Estrogen effect growth and reproduction at numerous physiological levels at target sites, including direct actions at the hypothalamic and pituitary levels to modulate GH production and secretion. In ovary-intact mice GH mRNA in the arcuate nucleus and Medial Preoptic Area (MPOA) had elevated, while ovariectomy decreased GH mRNA in both regions. When gonadectomized adults of both sexes were treated with estradiol, GH mRNA increased in females but had no effect in castrated males. It was also found that estrogen receptor-α is co-expressed in GH neurons in the MPOA and arcuate nucleus (Addison and Rissman, 2012).

There are some reports telling changes in GH level caused by stress and anesthesia, suggesting that, in blood sampling for GH assay, we should be careful not to give animals'unnecessary stress and avoid some anesthetics. Cold exposure for 5 minutes caused significant decrease in GH blood level to 43% of the onset level, and GH level was also decreased by 5 minutes' immobilization stress. Eight hours' immobilization a day for 10 days decreased GH levels, and GH level was further decreased by injection of GnRH+TRH during this period. GH level was increased by administration of ketamine (100mg/kg)＋Xylazine (10mg/kg) so that its activities will be impaired (Grondin *et al*., 2005).

2.7. Impacts of growth hormone on human, animals and environment

2.7.1. Impacts of growth hormones on carcass

Along with increasing in live weight due to HGP treatment, there is a corresponding increase in dressed carcasses weight. Carcass implanted with hormonal growth promoters has a higher ossification score but a 10 to 15% lower marbling score. The reasons for reduced marbling scores are unclear. Some have proposed that implantation of hormonal growth promoters early in an animals' life could delay the deposition of marbling, whereas others consider that it is due to the stimulation of increased protein deposition which effectively dilutes the fat content within the muscle (Lawrece *et al*., 2001).

Meat from HGP-treated animals does not improve as quickly during ageing, so an additional period may be required. Tender stretching (hanging by the aitch bone or sacrosciatic ligament) during chilling has been shown to provide great improvement in the tenderness of certain primal cuts. This will largely offset the effects of HGP treatment on carcass quality (Hunter, 2001).

There is an increased harmful health effect in dairy cows. Cows injected with rBGH have higher rates of 16 harmful medical conditions, including mastitis (udder infections), chronic diarrhea, reduced pregnancy rates, and lower birth weight of calves. It's use is opposed by the Humane Society of the U.S. Animal Protection Institute & Humane Farming Association (Kronfeld, 1993).

Recombinant Bovine Growth Hormone increases antibiotic use in animals and risk of antibiotic resistance in humans. Use of rBGH causes increased rates of mastitis in cows, leading to increased use of antibiotics. This contributes to higher levels of antibiotic resistant bacteria in food, air, soil and water, thus elevating the risk of antibiotic resistance in humans, a major concern in health care (Kronfeld, 2000).

2.7.2. Impacts of growth hormones on human**.**

Because of humans are in direct contact with the animals been eating and drinking their products, the outcome of this must be assessed in human beings too.So there is need for doing this.The long-term safety of increasing GH and IGF-I levels in aged people has become a concern because of reports of an association between serum IGF-I levels and cancer risk, especially of prostate, colon and breast. On the other hand, in acromegalic patients a GH-induced increase in serum IGF-I levels is accompanied by a parallel increase in serum IGFBP3 levels, which might have protective effects on tumoral cell proliferation ,unlike in normal ageing where IGFBP3 levels are generally reduced. At present, no deaths or increased cancer rates directly attributable to GH use have been reported in elderly people; this may simply reflect the short term clinical trials so far performed or the fact that this therapy is usually given toward the end of life, not allowing enough time to affect tumor development or growth, which is simply to indicate that there is short life expectancy for elders which is not possible to access the outcome of the therapy (Giordano *et al*., 2008).

It is now recommended that rhGH treatment not be initiated in patients with an acute critical illness. The cause of the increase in mortality is unknown; therefore, great caution needs to be exercised in the use of rhGH in adults outside the currently approved use in GH deficiency. The adverse effects of rhGH may be via either the direct or the indirect effects of GH. Initial experimental studies in animals suggest that metabolic or cytokine responses may be involved in these adverse effects. The recent suggestion of an increased incidence of type II diabetes mellitus in children who are treated with GH also indicates that rhGH-treated patients deserve close monitoring (Roelfsema and Clark, 2001).

2.7.3. Effects on the environment

The increased clustering and growth of CAFOs has led to growing environmental problems in many communities. The excess production of manure and problems with storage or manure management can affect ground and surface water quality. Emissions from degrading manure and livestock digestive processes produce air pollutants that often affect ambient air quality in communities surrounding CAFOs. CAFOs can also be the source of greenhouse gases, which contribute to global climate change (Schmalzried and Fallon, 2007).

The type of manure storage system used contributes to the production of greenhouse gases. Many CAFOs store their excess manure in lagoons or pits, where they break down anaerobically (in the absence of oxygen), which exacerbates methane production. Manure that is applied to land or soil has more exposure to oxygen and therefore does not produce as much methane. Ruminant livestock, such as cows, sheep, or goats, also contribute to methane production through their digestive processes. These livestock have a special stomach called a rumen that allows them to digest tough grains or plants that would otherwise be unusable. It is during this process, called enteric fermentation, that methane is produced. The U.S. cattle industry is one of the primary methane producers. Livestock production and meat and dairy consumption has been increasing in the United States, so it can only be assumed that these greenhouse gas emissions will also rise and continue to contribute to climate change (Burkholder *et al*., 2007)

Residues of growth promoting hormones are not remaining only in the meat that we consume but they also excreted with faces to the environment. Scientists are increasingly concerned about the environmental impacts of these hormonal residues as it leaks from manure into the environment and cause contamination of soil, surface and ground water. Aquatic ecosystems are particularly vulnerable to growth hormone residues and exposure to these hormonal residues has a substantial effect on the gender and reproductive capacity of fish (Schiffer *et al.,* 2001).

While manure is valuable to the farming industry, in quantities this large it becomes problematic. Many farms no longer grow their own feed, so they cannot use all the manure they produce as fertilizer. Ground application of untreated manure is one of the most common disposal methods due to its low cost. It has limitations, however, such as the inability to apply manure while the ground is frozen. There are also limits as to how many nutrients from manure a land area can handle. Other manure management strategies include pumping liquefied manure onto spray fields, trucking it off-site, or storing it until it can be used or treated. Manure can be stored in deep pits under the buildings that hold animals, in clay or concrete pits, treatment lagoons, or holding ponds (Hribar, 2010).

2.8. Economic Importance of Growth Hormone in Animal Production

Growth hormones implants are size neutral technology. Meaning that they do not exclusively benefit large scale cattle feeding operation and that they do not place smaller farm at a disadvantage (i.e whatever the level of the farm, every user of GH in its animal become beneficiary). Implants are approved for every stage of production in beef cattle from cow-calf farms, ranches rising and nursing calves to back grounding and stocker operation and feedlots of all size (Davies, 2000).

In the USA and many other countries, animals are commonly treated with hormones to increase production. Hormones are part of a range of treatments and feed additives that are or have been used to enhance growth, production and meat quality. The first hormones to be used as growth-promoting agents were natural estrogens and androgens, but synthetic anabolic steroids have also been used for a long time. Most of them are modified or derived from natural hormones. Zeranol is closely related to and synthesised from the mycotoxin zearalenone, known as a natural endocrine disrupter. The standard mode of treatment is by insertion of a slow release implant under the skin, behind one ear of the animal (Grotmol *et al.,* 2006).

Hormonal growth promotants are the natural sex hormones which are administered to animals in order to improve an animal's ability to use nutrients efficiently. Synthetic derivatives of the natural hormones may also be used instead of the natural hormones themselves (Canadian Cattlemen's Association and Beef Information Center, 2001).

2.8.1. In beef production

In the United States, hormones have been approved for use since the 1950s and are now believed to be used on approximately two-thirds of all cattle and about 90% of the cattle on feedlots. Cattle producers use hormones because they allow animals to grow larger and more quickly on less feed and fewer other inputs, thus reducing production costs, but also because they produce a leaner carcass more in line with consumer preferences for diets with reduced fat and cholesterol. Melengestrol acetate, which can be used to improve weight gain and feed efficiency, is approved for use as a feed additive. The U.S. Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA) cooperate in regulating growth promotants for livestock (Johnson, 2015)

Hormonal growth promotants, and the synthetic derivatives, are used to improve an animal's ability to use nutrients efficiently. Beef producers use hormonal growth promotants because they: improve meat quality by increasing the development of lean meat and decreasing fat content; increase feed efficiency, thereby allowing more growth with less feed; reduce costs for producers thereby reducing the price of meat and meat products for consume beef production in Canada competitive with other beef producing nations (Canadian Cattlemen's Association and Beef Information Center, 2001).

2.8.2. In dairy Production

In lactating dairy cows, somatotropin is a major regulator of milk production. In biology terms it is referred to as a homeorhetic control and acts to coordinate metabolism thereby allowing more nutrients to be used for milk production. This coordination involves most organs and tissues in the body, and includes the metabolism of all nutrient classes – carbohydrates, lipids, proteins, and minerals. Thus, rbST-supplemented cows produce more milk and utilize nutrients more efficiently. The net effect is an improvement in milk output per feed resource input, commonly referred to as an improvement in "productive efficiency". Productive efficiency is highest for a dairy producer's best cows and indeed, genetically superior cows make more somatopropin and have a greater productive efficiency (Bauman and Collier, 2010).

The use of Recombinant Bovine Somatostatin is initiated during the 9th or 10th week of lactation and continues until the end of lactation. Posilac is a plant oil formulation of rbST in which about 1-cc is injected subcutaneously (under the skin) at two-week intervals. There is some variation among individual cows and herds, but the typical response is a 4.5 kg (10 pounds) increase in a cow's daily milk yield. From a producer prospective the use of rbST makes all cows more like the best cows in the herd. There are no special nutritional needs other than feeding a balanced diet, and cows receiving rbST increase their voluntary intake to an extent needed to meet nutrient requirements. Comprehensive management programs related to nutrition, reproduction, and cow health are the same for cows of comparable production regardless of whether rbST supplements are used to achieve that production (Bauman and Dushea, 2005).

Dairy producers have been under pressure to increase their production because dairy prices have been quite volatile since the early 1980s, at times dropping so low that producers are unable to cover their production costs. During periods of low prices, dairy farmers tend not to reduce their production; after all, they cannot simply turn off their cows, and selling off such an expensive investment is not something farmers do lightly. Instead, they try to maximize production in order to spread their costs across as much output as possible (USDAERS, 2009).

3. Conclusion and recommendations

Growth hormones increase the growth rate, improve feed conversion efficiency, and enhance carcass quality when they are appropriately administered in animals into the correct sites with the correct dose. But now a day opposition against the use of growth hormones has increased because there is possibility in the formation of residues in edible tissues that might endanger to consumers by having carcinogenic effect, behavioral and reproductive changes to the animals, for consumers and can cause environmental pollution by passing with urine and faeces form treated animal. Currently it is possible to increase the growth rate and feed efficiency; and also possible to decrease fat content of the carcass by judicious choice of the animal breed, or by administration of natural or synthetic steroidal hormones with either estrogen or androgen activity. Natural hormones are testosterone, eostradiol and progesterone while synthetic hormones are melengestrol acetate, trenbolone acetate and zeranole which are widely used in different countries of the world.

In view of this conclusion the following out looks are forwarded;

- ❖ Growth hormones must be used properly in relation to their dose, site of administration and implanted by appropriate professionals.
- ❖ Farms which apply growth hormones as growth promoters must have appropriate waste retention and management program.
- ❖ There must be creation awareness on growth hormones in line with appropriate withdrawal period to the public.
- ❖ In Ethiopia context we should have appropriate waste disposal mechanism by taking in consideration its impact on aquatic organisms.

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