



Review Article

Vol 5 Issue 2 April-June 2021

LGU J. Life. Sci

ISSN 2519-9404

eISSN 2521-0130

Preamble of Steroids Types and Presence of Androgenic Anabolic Steroids (AAS) in Humans and Animals

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ABSTRACT: *Steroids are the hormones; the main source of which are Adrenal glands and Gonads. Human body produced them naturally in a balanced quantity. They have mainly two types i.e. corticosteroids and anabolic-androgenic steroids (or in short form "anabolic"). Now-a-days these are artificially synthesized as drugs which are given to humans and animals. Anabolic steroids are naturally produced in body 4.0–9.0 mg per day. They are also used artificially to treat testosterone level in human body while athletes are using them to build their muscles. Athletes misuse this drug 10 to 1000 times more than the medical purpose. These drugs (Oestradiol benzoate, Progesterone, Testosterone propionate, Zeranol, Trenbolone acetate, and Melengestrol acetate) are given to animals 0.25 to 0.5 mg on daily routine for increasing their body mass or meat production which is causing serious health problems in meat consumers. Glucocorticoids and sex hormones found in animal milk naturally. While their recombinant hormone rBGH is using to increase milk production in animals has become a part of serious health concern in public. This review entails the brief description on steroids history, types, use by humans and animals and also the harmful effects on human health.*

Key words: *Steroids, androgenic anabolic steroids (AAS), corticosteroids, meat and milk*

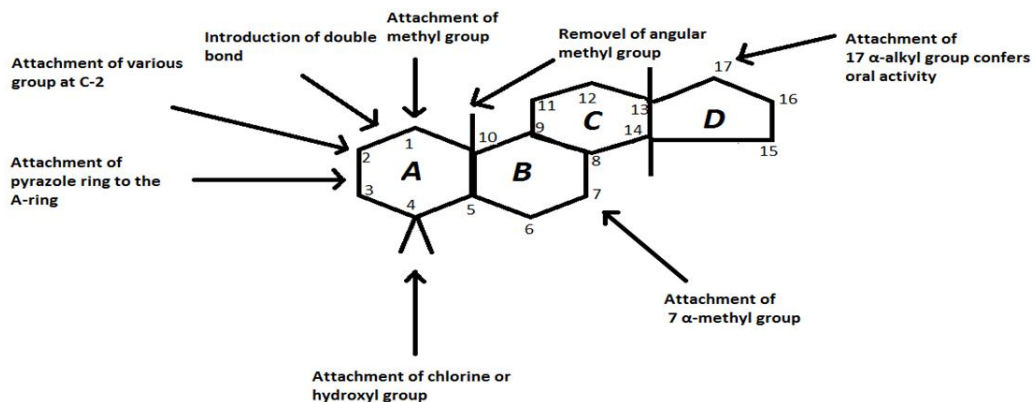
INTRODUCTION

Steroids are hormones produced by Adrenal glands and Gonads (Brown and Spencer, 2013). These are release in small fraction of the total amount of

steroids which produce by human body. But it decreases the activity of immune system and also decreases the level of protein and increases the fats in human body. Adrenal steroids produce by adrenal glands effect the body homeostasis,

nervous system, growth cells and also control the mineral metabolism and moderate the stress response. Sex steroids known as gonadal steroids are involved estrogen or androgen and progesterone receptors. These provide development of embryonic reproductive system and brain at birth and also control the reproductive behavior and sexual characteristics (Evans, 1988; Harvey, 2020). Steroids are biochemical structures made up of 17 carbons that are arranged in a specific molecular configuration with four rings. Basic structure of testosterone is composed of 3 rings of cyclohexane and 1 ring of cyclopentane with a group of methyl group at the opposite position of 10 and 13 (Srinivas and Wu, 2006).

both male and female (Rashid et al., 2007; Ainsworth, 2020). Humans are using these steroids for different purposes such as to boost their self-esteem, confidence and strength. Most of the users of these drugs are athletes. Anabolic steroids are top of the list. Apparently, these anabolic steroids seem to be really effective and beneficial for athletes but they have serious adverse effects (Kanayama and Pope, 2018). It is also used in animals and birds for food production. There are number of steroids has approved by Food and drug administration (FDA) for use in cow, buffalo and sheep. This is given to animals through their feed. Animal food is main source of cholesterol, protein, saturated fats and formation of steroid



IM = intramuscular

Fig. 1: In structure modification A- and B- rings that enhance the anabolic activity of the steroid molecules (Kicman and Gower, 2003).

Anabolic steroids or androgen steroids refer to testosterone. These are similar to the male testosterone hormone which provides growth of muscle and development of sexual characteristics in

hormones. These are given to animals for increase their data and weight of body. These are not harmful for animals and animal product such as (meat of animals or birds) safe for human to eat but the product is effective (FDA, 2014).

Steroids are used to increase the weight of birds such as chicken. Cholesterol, progesterone and estradiol cause the formation of testis and secretion of androgen testosterone and these factors effect the inhibition of luteinizing hormone secretion by anterior pituitary glands (Scanes, 1986).

History

Modern history of steroids starts from 20th century. Testosterone isolate in 1935 in Germany and in 1954 athletes start taking anabolic steroids for participating in Olympics (Wade, 1972). Androgenic anabolic steroids originally developed in 1958 in USA and in 1959 athlete Bill March use steroid for muscle growth. In 1960 Danish cyclist Knut Jensen have dead in Olympic competition due to 100 km trail race. His post mortem showed the traces of amphetamine (Graham et al., 2012). In 1967 Tom Simpson who was the British cyclist caused death by drug in the Tour de France. His post mortem showed the traces of amphetamine, alcohol and diuretic drug. Because two tubes of amphetamine and other few empty tubes are found in the pocket of racing jersey. In 1968 compulsory drug was control at winter Olympic Games in Grenoble. In 1969 the first radioimmunoassay (RIA) fluids was published for measurement of steroids. In 1974 the IOC Medical

Commission banned the development of androgenic anabolic steroids (AAS) due to the development of screen for the 17 α -alkylated active drugs in the biological medium of urine. In 1984 few Olympic team doctors explore the drug and prefer the athletes to use specific drug to increase the performance and fitness (Mottram, 1999). But 1980 it started to spread in general population. In 1990 begun the illegal selling of steroids and in 2004 expands the selling and formation of steroid (FDA, 2014). In 2008 steroids used by military and private secretary constructors in Iraq and Afghanistan. In Mexico and European nation steroids are available and smuggled without permission in united state. But in south Asia, America, Middle East, Africa and Asia use high amount of steroids in sport persons, teen agers, drug users and school students (DEA, 2004). Today more then 100 varieties of anabolic steroids have been developed. But just limited number of steroids has approved for human use.

Types of steroids

Adrenal glands lie on kidneys while gonads are reproductive organs of male and female. In males these gonads make Testies and in females ovaries and produce estrogen and progesterone. Adrenal glands produce 3 types of hormones (Ceccato et al., 2018).

Table 1: Types of different steroids and their functions

Steroid		Function	Example	References
Glucocorticoids		Anti-inflammatory drugs	Cortisol	(Schäcke et al., 2002; Ceccato et al., 2018)
Mineralcorticoids		Regulation of blood pressure	Aldosterone	(Ceccato et al., 2018)
Androgen Steroids	Anabolic	Produce characteristics	Male Testosterone	(Rashid et al., 2007)

Limits of Steroids

Testosterones are produced by pituitary gland and production of testosterone is under control of Luteinizing Hormone. Approximately production of testosterone in healthy men is 4.0–9.0 mg per day with the range of 300 to 1000 ng/ dL⁻¹ of blood concentration.

On other hand female have 15 to 65 ng/ dL⁻¹ range from blood concentration (Hoffman et al., 2009). The limit of anabolic receptor and nuclei cell can take steroid in fully amount at once then they can not take any more amount of steroids. If in animals given to 10 time original doses of steroids have no harmful side effects. But in human these amounts of dose have excessively harmful side effects. If increases the amount of dose then it is not build the muscle development. Some athletes take anabolic steroids artificially to gain strength and for good performance. If they use steroids regularly for 3 weeks then growth pattern is developed. Other hand, if they gain 5% dose 6 to 8 weeks then it is difficult to build muscle development. So, its limit has no beneficial for human body. Less amount of dose is 3% which shows good result for human. But, when left the use of

steroids then it has enhance the harmful side effects such as loose body weight, dehydration in few weeks (Lenehan and Kemplay, 2004). Athletes prefer lower amount of dose 10 mg or high amount of dose 25 mg of methane dienone per day. These procedures conduct continually for six-week with methane dienone randomly and unreliable methodology shows that diminish the effect of steroids after continually treatment (Imhof, 1998).

Harmful effects on humans

Many kinds of drug are used by humans in which anabolic androgenic steroid is top of the list. Apparently, these anabolic steroids seem to be really effective and beneficial for athletes but they have serious adverse effects such as liver damage, heart attacks, kidney failure. It can lead to depression if someone stops using this drug. Anabolic androgenic steroids enhance the testosterone hormones and produced strong male characteristics. Testosterone hormone is 90% lower in females than males (Goodman, 1996; Rashid et al., 2007). That's the reason they don't build muscles like men so, these androgenic anabolic steroids can enhance the development of muscles in both men and women. A control amount of this drug can be

benefitted in many cases such as to treat weak muscles, men having lower level of testosterone hormone and other sexual issues in men (Shahidi, 2001; Rao et al., 2017). People who use steroids especially body builders has an ultimate goal to achieve muscles size and strength so this is one of the reason they don't follow any advice or any prescription given by health consultant. The amount taken by people to misuse this drug can be 10 to 1000 times higher than the amount use for medical purposes (Trenton and Currier, 2005; Striegel et al., 2006). This drug can be taken intramuscularly, orally and can be applied on the skin as they found in form of cream and gel (American Academy of Pediatrics, 1997; Medline Plus, 2016). Steroid abusers use many techniques to get maximum results and to minimize the adverse effects such as "stacking" in which they use different combination of anabolic androgenic steroids in a 4-12 weeks cycle, including a period in which they stop taking steroids. Similarly, another mode user adapt is "pyramiding" which involves 6 to 12 week cycle at first they start with a very low dosage and then gradually increase the amount and then get to the maximum dosage then again decrease in dosage (Blue and Lombardo, 1999). Some steroid abusers also use "plateauing" to prevent tolerance for specific steroids so after using a steroid for a specific period they replace it with another steroid (Yesalis, 1992). Aggression is somehow related to the male characteristics and testosterone level. Aggression is one of the major

adverse effects found in steroid abusers and they report more aggression than non-users (Burnett and Kleiman, 1994). In an experiment it was observed that AAS users show more anti-social attitude and more fights and more violence and involvement in dangerous activities (Cooper and Noakes, 1994). The greater amount of this dose produces more aggression and more irritability than lower one (Bahrke et al., 1996). Several studies have shown no significant effect of steroids on aggressiveness and behavior (Tricker et al., 1996). Researchers have concluded that not all the anabolic steroids effect on behavior and aggressiveness. AAS produce feelings of anxiety and cause depression and mood swing. Psychological effects vary with the dosage of steroids (Pope and Katz, 1994; Ip et al., 2012). Research also shows that some steroid abusers can turn to other drugs. In a study of 227 people addicted to different drugs like heroin and opioids, it was found that 21 people had used anabolic steroids in the past activities (Arvary and Pope, 2000). Another study conducted on men who were addicted to opioids, 25% of them used to take steroids then they turn to other drugs (Kanayama et al., 2003). Like most of the countries in Pakistan a large number of body builders are using steroids. In a study of 310 males body builders within Islamabad and Rawalpindi between age group of 15-35 years, 64% reported the use of anabolic steroids and 83% of them was using steroids in injectable form. The shocking thing is

72% were aware of adverse side effects of anabolic steroids on health. 62% knew that it is illegal to use steroids. Major source of information and motivational forces that make them feel like they need steroids were 52% trainers, 26% friends, 13% internet and rest 8% magazines and newspapers (Usman et al., 2015).

Harmful effects on humans through animal meat and milk

From meat:

Growths promoting hormonal substances are Oestradiol benzoate, Progesterone, Testosterone propionate, Zeranol, Trenbolone acetate, and Melengestrol acetate (Bircher et al., 2015). These are using to increase cattle body weight, feed efficiency, protein storing efficiency and reduced fat (Moran et al., 1991; Cecava and Hancock, 1994; Sawaya et al., 1998). Progesterone is a sex hormone. It's produce in the ovaries. It's involved in the reproduction cycle and development of mammary glands in humans as well as in animals (Zalanyi, 2001; Conneely et al., 2000). Melengestrol acetate (MGA) is progesterone. It's given to animals as their feed which helps them to gain their body weight (FDA, 2013). MGA dose is given about 0.25-0.50 mg on daily routine about 90-150 days before slaughter according to Canadian food inspection agency. It causes reproductive toxicity as well as carcinogenic for human health (Nachman and Smith, 2015). Diethylstilbestrol (DES) is a non-steroidal estrogen like estradiol. It's used as growth promoter in animals. It's also used to treat

hypothyroidism and hormonal imbalance (Yang et al., 2013). Many studies showed that it's mutagenic, carcinogenic and teratogenic and causing many public health concerns (Andersson and Skakkebaek, 1999; Chuanlai et al., 2006; De Brabander et al., 2007). High level of estrogen in red meat is causing breast cancer risk in females (Cho et al., 2006). Oestradiol and Testosterone are deposit in the muscle, liver, kidney and fat of animals (Sangsrivong, 2003). Derivatives of these hormones cause abnormal cell growth, gene disorder and DNA damage (Hoffmann, 1981; Metzler and Pfeiffer, 2001; Stepniak and Karbownik, 2016). Conventional broilers are fed on commercial feed while the organic broilers are fed on the natural grains (Ahmad et al., 2018). Recent study showed that commercial broiler feed contains some antibiotics and noxious additives including roxarsone and steroids (Mangalgi et al., 2015). Excessive use of these drugs in the animals feed cause serious health problem for the consumers (Seri, 2013). While the presence of antibiotics in the organic chicken meat was not observed (Ahmad H and Ahmed I, 2015). The use of these steroids in animals through their feed or injections is highly toxic for human health.

From Milk:

Cow's milk contains much kind of steroid and protein hormones. Steroid hormones in milk are glucocorticoids and sex hormones. In sex hormones progesterone, 17 β - estradiol (E2), estrone (E1), and estradiol (E3) are included

(Canapana and Baunarucker, 1995; Jouan et al., 2006; Pape-Zambito et al., 2010; Macrina et al., 2012). Protein hormones in milk are insulin-like growth factor-I (IGF-I), prolactin, bovine somatotropin and gonadotropin-releasing hormone (Vicini et al., 2008). Recombinant bovine growth hormone (rBGH) or bovine somatotropin (BST) is genetically synthesized protein which is used to increase the milk production in the cows (Girma et al., 2014). BST increases milk production in cows 10 to 15% (Hoagland et al., 1997). Production of rBGH stimulates the activity of another hormone insulin-like growth factor (IGF-1) which produced by liver and mammary gland (Chilliard et al., 2001). Several studies showed that rBGH is not responsible for human health problems but it activates the production of IGF-1 which increases the milk production (Slaba et al., 1994; European Commission, 1999). It reveals that increased level of IGF-1 is associated with several type of cancers such as prostate, breast, colon-rectum and lung (Li et al., 1998; Yu and Rohan, 2000; Wei et al., 2015).

CONCLUSION

The use of these growth promoting hormonal substances are harmful. They are beneficial only in the treatment of diseases according to the health consultant's prescription. But their excessive use in humans and animals is a very serious matter of public health concern. Presence of these drugs in animal meat and milk just for the sake of

increased amount of meat and milk are becoming toxic for their consumers. At present it is direly needed to explore about AAS as there is little knowledge available about its use and dependency in animals and humans. The risk factors are still to be understood well for AAS dependency. The public awareness regarding its illegal use of these steroids should be monitored strictly.

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