THE ECONOMICAL AND TECHNOLOGICAL ASPECTS OF THE ANABOLIC USE IN MEAT PRODUCTION AND THEIR IMPLEMENTATION ON HUMAN HEALTH

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ABSTRACT

Anabolic agents have been used through the world in the production of food animals for more than 40 years. The main reason for their use is the fact that anabolic agents increase the fixation of nitrogen, what make more effective the process of accumulation of proteins in animal body. But, the overall effect of anabolic use in meat production measured in terms of increased average daily weight of animal, improved feed conversion efficiency, better conformation of carcasses, increased protein to fat ratio, etc. Countries - members of European Union prohibit the use in stockfarming substances having a hormonal and thyreostatic action and β-agonists. In other countries, like USA and Canada, the use of natural hormones in animal breeding is permitted. No study has evaluated the effects of anabolics as growth promoters in farm animals on cancer occurrence in humans. But, meat consumption seems to be associated with increased risk of breast and prostate cancer. The studies conducted on vegetarians, and many other studies, confirm the statement that overall cancer risk is generally lower among less meat consumers. The first priority for public health protection is to prevent the illegal use of banned products by performing monitoring programmes at farms and slaughter houses and by developing and applying sensitive and reliable analytical methods for residue analysis.

Key words: human health, meat production, anabolic agents

INTRODUCTION

For humans, meat is an excellent source of proteins for building and repairing body tissues, fats for energy and heat requirements, minerals for building bones, teeth, blood and for regulating the body, vitamins for promoting growth and health etc. (Hinmand and Harris, 1947).
The first half of 20th Century brought about positive attitude concerning the contribution of meat to human health. A great deal of research established the nutritional benefit of consuming meat. Fat in meat was considered as an energy source. But, the second half of

past Century carried out a negative attitude about meat consumption and human health. Al that time scientific data indicated that the saturated fatty acids, predominantly presented in meat, were associated with cholesterol level in human body and with coronary heart disease (Cassens, 1999).
From that time consumers started to be concerned about the quality of their food. Low caloric food, e.g. food with low fat content, started to be a pattern of healthy life style in developed countries. The meat industry responded to this consumer demands for meat with lower fat content in two ways: by breeding much leaner animals and by manipulating of growth in farmed animals. The second way became of high business interest and new "pathologic" technologies started to be introduced in animal rearing.
Concern about the food contamination led to a fear about health and safety aspects of food. An important consequence of the food scare period was the rapid demand for healthy food, but meat still does not have the image of healthy food (Sardi 2000). Of all pharmaceuticals, the use of anabolics and other different type of drugs as growth promoters in the last twenty years were the most heavily discussed topics and of the greatest publics health concern in Europe, as well as in many other countries around the world. Data of Jolly et al., 1989. indicate that residues are of the primary concern about food risk components amongst consumers in California, followed by irradiation and fat. It is evident that at the end of the 20th century consumers started to be more disturbed by presence of residues in food than by the fat content of it. They became aware of the very harmful effects of different type of residues in food on their health more than about fat content related to cholesterol level in the blood. Since the time when the overall cancer risk was related to meat consumption, especially to hormone - treated meat consumption, the consumers started to consider the hormones and other anabolics of the first potential risk to their health.
Anabolic agents have been used throughout the world in the production of food animals for more than 40 years. The main reason for their use is the fact that anabolic agents increase the fixation of nitrogen, what make more effective the process of accumulation of proteins in animal body. But, the overall effect of anabolic use in meat production in measured in terms of increased average daily weight of animal, improved feed conversion efficiency, better conformation of carcasses, increased protein to fat ration, etc. (Van Veerden, 1984; Schmitz et al., 1990; Sainz & Cubbage, 1997). In general, the anabolic effects relates to type of animal (ruminants, pigs, poultry, fish, wild farmed animals etc.), to sex, age, to type or combination of compounds used and to the given dose.
In animal breeding there are three main classes of agents used to manipulate growth: hormones, β-agonistic drugs and feed additives.

HORMONES

The compounds with anabolic effect, first of all hormonal preparations, have been legally used in fattening animals all over the world until the early 80s (FDA, 1980; Council Directive EEC, 1981). After the acquired knowledge on their toxicological properties (teratogenic and carcinogenic) first to be prohibited, in the world, was the use of stilbenes and its derivatives. Than the EU member countries prohibited the use of all other hormones, thyrostatics, β-agonists and other compounds with anabolic effect in animal breeding whose meat is intended for human nutrition. From that time the control of their residues is obligatory (Council Directive EEC/469, 1986).
The mechanism of hormonal action which, unlike other compounds (antibiotics and chemotherapeutics), has a real anabolic effect is expressed through influence on inter-

mediary metabolism, that is anabolic and catabolic processes. The balance is disturbed, and that is reflected in redistribution of nutrients from fatty to muscle tissue. As a result, the weight gain of animals by unit of weight of consumed food increases. Apart from its positive role in growth stimulation, the use of hormones may have also an unfavourable effect on the quality of meat, what especially affects the tenderness and marbling. However, hormones do not have a remarkable positive or negative effect on parameters of carcass quality, like colour, pH, the contents of protein, collagen, dry matter, water binding capacity, etc. (Apple et al., 1991; Bartle et al., 1991; Gerken et al., 1995).

Nowadays, there are various opposite opinions on toxicological properties of hormones, potential human health hazard and economic effects that can be achieved by their application. What is indisputable in this matter is the ban on use of stilbenes, which were widely used in animal breeding until the late 70's. Their strong estrogenic activity, the fact that they do not break down in animal liver, possibility of their residues to enter the food chain as well as their toxic properties (mutagenicity and carcinogenicity) caused the ban on their use in meat production. In the countries, members of European Union (EU) the Council Directive No. 96/22/EC prohibits the use in stockfarming certain substances having a hormonal or thyrostatic action and of β-agonists. The Council Directive 96/23/EC issues the measures to monitor certain substances and residues thereof in live animals and animal products. In other countries (USA, Canada, etc.), which are large meat producers the use of natural hormones (estradiol, progesterone, testosterone) is permitted in animal breeding. The use of other, like trenbolone, zeranol and melengestrol acetate, is legal but with appropriate control (USDA, FSIS, 1992; Galbraith, 2000). Table 1. shows hormones permitted for use in USA in cattle, sheep and poultry production. Apart from melengestrol acetate, whose is applied orally through food, in the dosage of 0.25-0.5 mg/day, all other compounds are applied as implants. Depending on the purpose, there are different combinations of the above mentioned hormones, in different concentrations, up to several hundreds of milligrams. According to the regulations, the pellets are implanted subcutaneously, behind the ear. If applied illegally, they are implanted into places where their detection is difficult. Different species might react differently to hormones. The main reason for application of hormones is growth promotion and obtaining of extra proteins during the period of fattening, that is based on the increase of feed conversion ratio (anabolic effect). These effects are mostly expressed in ruminants and account for 10-20%. Hormonal preparations, especially the compounds with estrogenic activity were also used in poultry production. Their application affected the growth promotion to a lower extent and more to the conversion of fat into the muscle tissue (Hoffman, 1978). The effects of application of different hormonal preparations in pigs were marked as the increased lean to fatty tissue ratio, but the weight gain in animals was not significant (Flower, 1976; Van Weerden and Grandadam, 1976). In general, the anabolic effects depend on the sex, age and species, kind and composition of hormonal preparations and the applied dose (Heitzman, 1976).

In the countries where hormones are permitted in the stockfarming, there is opinion that, since they degrade in liver, these hormones do not have residual activity and thus not hazardous for human health. On the other hand, their ingestion through meat of treated animals is lower than 8% of total intake through food (dairy products, plant estrogens, meat of untreated animals, etc.) (WHO, 1982). Table 2. shows human intake of anabolic steroids from meat compared with their endogenous production in humans at various age.

Potential cancerogenicity and other toxic effects of hormones are discussed from the aspect of acute exposition to high doses as well as chronic exposition to small doses over the long

period of time. The exposition to high doses originates from a wide medicinal application of hormones (oral contraception, postmenopausal therapy, application during pregnancy etc.). At the moment there are no data on the exposition of population to low doses of estrogens. **C**hildren, until the puberty, are about 20 times more sensitive on estrogens intake than the adults. Induction of the estrogenic effects in children (signs of early puberty) depends, not as much on the single dose, but on the duration of exposition (WHO, 1982).
The literature data indicate that the highest potential risk from the intake of high quantities of hormones comes from the consumption of meat from the point of the implanted palette, where their concentration is the highest (WHO, 1982; Van Weerden et al., 1984). However, there is no information in the literature that would directly indicate the correlation between the use of hormones as growth promoters in the animal breeding and the incidence of carcinoma in humans. The attention is mainly paid to hormones as the causing agents of carcinoma in general. Many studies suggest the correlation between the mammary and prostate carcinoma with higher degree of meat consumption, especially red or processed meet (EC Opinion of the scientific committee on veterinary measures relating to public health, 1999). Namely, these data indicate that the highest rates of breast cancer are observed in North America, where the consumption of meat from hormones treated animals is the highest in the world.
Although the opinions on the use of hormones as growth promoters are opposing, the reported data suggest that, in order to protect the public health, the most important thing is to control the use of hormones by conducting the monitoring of their residues in live animals on farms and in the tissues of slaughtered animals.

β-AGONISTIC DRUGS

The ban on the use of hormones in the EU member countries, severe control of their application, market and nutritive aspects in meat production still imposed the more economical production and reduced fat contents in animal carcasses. All this, in the late 80's, brought about illegal use of a new generation of drugs in animal breeding in the countries of Western Europe. Among them are β-agonists (klenbuterol, salbutamol, mabuterol, cimaterol etc.), (Baker and Kierman, 1983; Baker et al., 1984), also known as repartitioning agents because of their property to selectively direct the use of energy derived from food towards the synthesis of proteins in muscle tissue on account of fat depots formation. The main advantage of these compounds, compared with the anabolic steroids is possibility of oral administration through animal feed. Anabolic properties of β-agonists are expressed if the administered doses are 5-10 times higher than the therapeutic ones i.e. over 1 mg/kg animal body weight per day, or 0.25-4 mg/kg feed, depending on the species. A significant improvement in efficiency of feed conversion is demonstrated in cattle, sheep, pigs and poultry (Jones et al., 1985; Allen et al., 1987;). The effects of application of β-agonists in pigs are: reduced feed intake, higher conversion rate, increased daily gain, increased protein to fat ratio, without significant changes in carcass weight (Dazzi et al., 1991).
β-agonists are, by their chemical nature, substituted phenylethanolamines, with structure and pharmacokinetic properties similar to catecholamines - adrenaline and noradrenaline. They are promoters of β-2 adrenergic receptors and are used in human medicine as cardiacotonics, bronchodilatators for curing asthma, and in veterinary medicine for induction tocolysis in cows because binding of β-agonists to β-2 adrenergic receptors results in relaxation of smooth musculature. Klenbuterol is illegally used also as doping

agent for racing horses. Illegal use of β-agonists in fattening animals as agents of repartition is well studied, but the mechanism of repartition of nutrients from muscle into fatty tissue is not completely explained. However, the effects of the use of klenbuterol cease after the treatment was finished and accelerated fat deposition occurs in treated animals. The authors conclude that every economic gain due to illegal use of klenbuterol (the increase in muscle weight, reduced fatty tissue) diminishes before the concentrations of its residues in tissues, relevant for the control, fall below the detection limits (Elliot et al., 1993a, 1993b; Sauer et al., 1994,1995).

The use of β-agonists in animal rearing may result in unwanted residue findings in tissues. Although metabolism and toxicity of β-agonists are still not studied enough, they represent a threat for human health (Ricks et al., 1984; Mayer and Rinke, 1990; Kim et al., 1992), and are considered more hazardous for the consumers than majority of the hormones. Their residues in edible animal tissues, by the intake into the human organism, may cause a tachycardia, muscle tremor, fever, headache, vomiting etc. (USDA-FSIS, 1995). Since the use of β-agonists in animal production is prohibited, and possibility of illegal use is considerable, the control of their residues in animal tissues is mandatory in the national residue programme.

FEED ADDITIVES

Besides hormones and β-agonists, some drugs are used not only in prophylactics and therapy, but also as additives in animal feed, or in animal drinking water in order to improve the feed conversion ratio and achieve better gain. As additives they are added in animal feed or water in small quantities, measured by ppm, over a longer period of time. It has been noticed that the use of drugs may improve the feed conversion by 17% in fattening cattle, 10% in lambs, 15% in poultry and 15% in pigs (Čupić, 1997). Unlike anabolics, the drugs do not affect physiological state of animals, or metabolic processes, but influencing the microflora they increase the absorption of nutrients from feedingstuff in the digestive tract. In our country the following drugs are registered : antibiotics - lincomycin chloride and streptomycin sulphate - for administration through drinking water in turkeys, ionoform antibiotic - monensine - for administration through feed for calves and lambs and chemotherapeutic – carbadox – for the use through feed for pigs (Valčić, 1995).

When feed additives are legally used, a good veterinary practice should be applied. A long-term intake of residues of any drug into human body might cause unwanted effects on human health.

WHO (World Health Organisation) and FAO (Food and Agriculture Organisation) recognise residues of veterinary drugs in food as one of the major public health concern. Programmes to monitor residues of environmental contaminants, like toxic elements, pesticides PCB's, etc., in tissues of food producing animals; to control the legal use of sulphonamides and other drugs, and the illegal use of anabolic agents and of the unapproved compounds in animal breeding are required to be included in the national regulations to be performed by authorised laboratories and supervised by the relevant authorities.

An effective programme should include; examination of excreta from animals, feeding stuff and drinking water on the farms; monitoring of residues in excreta, bile and tissues at the slaughterhouse from animals of known origin; (in case of positive results, back tracing should be applied and the reason for violation should be established and eliminated);

development and use of sensitive - screening and reliable- confirmative methods for detection of very small amounts (ppb and less) of compounds of interest.

Table 1. Hormones approved for use in USA and their maximal residue limits in animal tissues (USDA, FSIS, 1992)

COMPOUND	MRL (mg/kg)		
	CATTLE	SHEEP/GOATS	POULTRY
Estradiol benzoate	480 F	600 F	-
	360 K	600 K	-
	240 L	600 L	-
	120 M	120 M	-
Estradiol monopalmitate	-	-	0,002 ET
Melengestrol acetate	0,025 ET	-	-
Progesterone	12 F	15 F	-
	9 K	15 K	-
	6 L	15 L	-
	3 M	3 M	-
Testosterone propionate	2,6 F	-	-
	1,9 K	-	-
	1,3 L	-	-
	0,64 M	-	-
Trenbolone	TOLERANCE NOT NEEDED		
Zeranol	150 M	0,020 ET	-
	450 K	-	-
	300 L	-	-
	600 F	-	-

KEY:
M-MUSCLE *ET-EDIBLE TISSUE* *F-FAT*
K-KIDNEY *L-LIVER*

Table 2. Human intake of anabolic steroids from meat compared with their endogenous production in humans at various ages (REID, J.F.S., 1980; HENDRICKS, D.M., 1981)

	Testosterone	Estrogen	Progesterone
Production in humans µg/day)			
Adult male	6.480	136	416
Women			
- range during cycle	240	190-1600	418-19.600
- late pregnant	320	64.300	294.000
- post menopausal	140	46	326
Pre-pubertal child	32	42	150
Max. amounts of hormone (µg/200g meat)			
Untreated cattle	0,13[a]	0,11[b]	2,5[b]
Treated steer	0,0006	0,05	0,15
Treated hifer	0,025	0,05	-

a-mature bull
b-pregnant cow

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