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# Chemicals and drugs residue in meat and meat products and human health concerns

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ABSTRACT

Chemical contaminants comprise hazards which can occur in animal production, slaughter, processing or packaging. This paper was aimed to study those contaminants which are of most threat to animal origin food products. Livestock and veterinary services are responsible for contaminants and veterinary drugs residues, heavy metals, mycotoxins and pesticides that may be found during animal breeding. The most important contaminants which may be found in meat products are antimicrobial drugs, hormonal growth promoters, pesticides, heavy metals and added chemicals. When the veterinary drugs are ingested, they maintain sufficient activity after incubation in rumen fluid and can appear as residues in meat products potentially. Nevertheless, chemical contaminants are considered to be very important regarding to the consumer's confidence and human health concern, and reducing the occurrence in foods is demanded. Furthermore, surveillance programs and periodic reassessment of risks resulted from these contaminants is required to detect problems, therefor, proper corrective actions can be conducted for public safety.

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## 1. Introduction

We all consume many hundreds of different chemicals in our food every day. Some of these chemicals are food chemical structure and other are residues from chemical contamination in food such as meat products. Therefore, chemical contaminants are substances which are not intentionally added to food. They can present as a result of the production including operations carried out in crop husbandry, animal husbandry and veterinary medicine, manufacture, processing, preparation, treatment, packaging, transport and food holding, or as a result of environmental contamination or its production by a living organism (1). Chemical contaminants cannot reproduce outside a specified life cycle (2).

Some food borne pathogens such as *Listeria spp.*, and *Salmonella spp.*, isolated from meat products were resistant to multiple antimicrobial agents (cefotaxime, cefoxitin, tobramycin, amikacin, chloramphenicol, tetracycline, and erythromycin) (3) and ampicillin, chloramphenicol and tetracycline (4), respectively. In other research, antibiogram of *Escherichia coli* isolated from meat products revealed that majority of the isolates were resistant to doxycycline, cloxacillin, carbenicillin, penicillin-G and polymyxin-B (5). The appearance of substantial resistance to antibiotics in foodborne pathogen isolates shows the existence of antibiotic residues in meat products.

Different types of compounds may be found as contaminants in meat products including:

1. Chemicals used in crop production such as insecticides, acaricides, herbicides and fungicides.
2. Chemicals used in animal production such as antibiotics, hormones and growth promoters, repartition agents and insecticides.

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3. Environmental contaminants such as dioxin, polychlorinated biphenyls, heavy metals, radionuclides and mycotoxins.
4. Others such as nitrosamines and components from packaging materials.

Chemical contaminants in meat products are known to contribute in several diseases such as cancer and heart disease. Also, they can be involved in other diseases such as Alzheimer's disease and Parkinsonism (6). Synthetic chemicals such as DDT are major contributors to human cancer. So, pesticides can be a factor for causing cancer in human (7). Synthetic preservatives are used in food industries to improve the quality properties and also extend the shelf life of food products during storage. Although, the most common technological methods for preservation may not always protect against spoilage (8). This study aimed to review some major chemicals and drugs in the meat products.

## 2. Sources of chemical contaminants

Chemical contamination can occur during food chain. The sources of animal originated chemical contaminants in raw materials are comparable to those of originating from plants (9). Chemical compounds used for crop production are acaracides, herbicides, insecticides and fungicides which are used in crop and feedstuffs production. Some insecticides are used to control the flies on livestock. A lot of synthetic herbicides, fungicides, acaracides, and insecticides have been developed. These compounds may occur as residues in feed stuffs following with ingestion to animals and, thus, have a potential to contaminate animal tissues. Most are rapidly metabolized by animals, broken down or excreted (9,10). Insecticides like chlorinated hydrocarbon such as DDT, lindane, heptachlor, aldrin, dieldrin, and chloradane can accumulate in fatty tissues (11,12) and then the use of these compounds has been severely restricted. Polychlorinated dibenzodioxins (PCDDs), dibenzofurans (PCDFs), and biphenyls (PCBs) emitted from combustion sources. One of the most serious chemicals, are polychlorinated biphenyls. These were used as electrical transfer oils, in copy paper, and in many other uses. These compounds are chemically chlorinated hydrocarbon insecticides and behave in much the same manner in the environment. like the chlorinated hydrocarbon insecticides, these compounds are concentrated in fatty tissues of animals and may be concentrated to toxic level. Dioxins are somewhat similar types of chlorinated compounds. The residues of these chemicals have been detected in air, soil, sediment, fish, meat and meat products, dairy products, human tissue, and mother's milk (12,13).

Ghindini et al. (2005) compared the contaminant and residue levels in organic and conventional meat products from Northern Italy. They announced that pesticides and PCBs residues in both organic and conventional meat were lower than legal limits (14). Reinik et al. (2007) reported that the highest total Polyaromatic hydrocarbons (PAH) concentrations detected in Estonia were 16 μg $kg^{-1}$ in smoked meat and ham, 19 μg $kg^{-1}$ in smoked sausage and 6.5 μg $kg^{-1}$ in smoked chicken samples. Smoking and grilling are major cooking methods in Estonia, so meat products were evaluated in overall PAH intake (15).

In a research, Abedi et al. (2011) determined lead and cadmium content in cooked beef sausages, probably originated from feed. Results showed that the metal content, varied from 24.0 to 158.7 μg $kg^{-1}$ with an average of 53.5 for lead and from 2.2 to 13.5 with an average of 5.7 for cadmium. The highest lead and cadmium concentrations were obtained from a German sausage (158.7 μg $kg^{-1}$) and a hot dog (13.5 μg $kg^{-1}$) respectively (16).

## 3. Chemicals and drugs in animal production

Chemicals and drugs used in animal production include antibiotics and those to control diseases (10,11,12,17) parasites, natural and synthetic anabolic hormones, natural and synthetic growth hormones, and repartitions agents such as beta agonists and tranquilizers that increase the ratio of lean to fat in animals (12). These drugs may result in residues appearing in meat and meat products. Residues of some veterinary drugs in animals and foods has been shown in Table 1.

Some drugs like dexamethasone (DEX) has been used to treat inflammatory disease for its anti-inflammation, anti-endotoxin, low dose and slight sodium retention. Also, DEX promotes animal growth, because it improves feed conversion rate.

**Table 1.** Residues of some veterinary drugs in animals and foods.

| Types of products | *MRLs in Tissue (μg/ kg) | **ADI (μg/ kg body weight) | Species | References |
|---|---|---|---|---|
| Antimicrobial agents: | | | | |
| Ceftiofur | 1000 (muscle), 2000 (liver), 6000 (kideny), 2000 (fat) | 0 - 50 | Cattle, pigs | (FAO/WHO, 1998) |

| | | | | |
|---|---|---|---|---|
| Flumequine | 500 (muscle), 1000 (liver), 3000 (kidney), 1000 (fat) | 0-30 | cattle, pigs, chickens | (FAO/WHO, 1998) |
| Spiramycin | 200 (muscle), 600 (liver), 300 (kidney), 300 (fat) | 0-50 | cattle, pigs | (FAO/WHO, 1998) |
| Gentamicin | 100 (muscle and fat), 200 (liver), 1000 (kidney) | 0-4 | cattle and pigs | (FAO/WHO, 1995) |
| Neomycin | 500 (muscle, liver and fat), 5000 (kidney) | 0-30 | cattle, goats, pigs ,sheep, chicken | (FAO/WHO, 1995) |
| Chlortetracycline, Oxytetracycline & Tetracycline | 100 (muscle), 300 (liver), 600 (kidney) | 0-3 | cattle, pigs, sheep, poultry | (FAO/WHO, 1997b) |
| Benzyl penicillin | 50 (muscle, liver, kidney) | 30 | all species | (FAO/WHO, 1997b) |
| Sulfadimidine | 300 (muscle, liver, kidney & fat) | 0-4 | all species | (FAO/WHO, 1997b) |
| Growth promoter: | | | | |
| Trenbolone acetate | 2 (beta- trenbolone in muscle) 10 (alpha-trenbolone in liver) | 0-20 | all species | (FAO/WHO,1990) |
| BST | Not specified ( muscle, liver, kidney, fat) | Not specified | cattle | (FAO/WHO,1997b) |
| Anti-parasite agents: | | | | |
| Moxidectin | 20 (cattle muscle), 50 (sheep muscle), 100 (liver), 50 (kidney), 500 (fat) | 0-2 | cattle, sheep | (FAO/WHO,1998) |
| Thiabendazole | 100 (muscle, liver, kidney, fat) | 0-100 | cattle, sheep, goats, pigs | (FAO/WHO,1998) |
| Albendazole | 100 (muscle, fat), 5000 (liver, kidney) | 0-50 | cattle, sheep | (FAO/WHO, 1997b) |
| Febantel | 100 (muscle, fat & kidney), 500 (liver) | 0-10 | cattle, sheep, pigs | (FAO/WHO, 1991) |
| Febendazole | 100 (muscle, fat & kidney), 500 (liver) | 0-25 | cattle, sheep, pigs | (FAO/WHO, 1991) |
| Oxfendazole | 100 (muscle, fat & kidney), 500 (liver) | 0-4 | cattle, sheep, pigs | (FAO/WHO, 1991) |
| Closantel | 1000 (muscle, liver), 3000 (kidney, fat), 1500 (muscle, liver), 5000 (kidney), 2000 (fat) | 0-30 | cattle | (FAO/WHO, 1997b) |
| Levamisole | 10 (muscle, kidney, fat), 100 (liver) | 0-6 | cattle, sheep, pigs, poultry | (FAO/WHO, 1997b) |
| Insecticides: | | | | |
| Cyfluthrin | 20 (muscle, liver, kidney, fat) | 0-20 | cattle | (FAO/WHO, 1998) |
| Fluazuron | 200 (muscle), 500 (liver,kidney), 7000 (fat) | 0-40 | cattle | (FAO/WHO, 1998) |

* MRLs= Maximum Residue Limits.
**ADI= Acceptable Daily Intakes.

Obesity, hypertension, high blood sugar and osteoporosis are some side effects of redundant DEX in the human body. The MRLs of DEX in pork muscle and pork liver was 0.75 ng/g and 2 ng/g, respectively, established by the Ministry of Agriculture of the People's Republic of China No. 235, 2002 (18).

### 3.1. Anti-parasite drugs

Anti-parasite drugs used for removing internal parasites such as flukes, tape worms (helminths) and nematodes (round worms) have an important role in animal production. The closantel and rafoxanide are active against Fasciola hepatica (liver fluke) (19) and albendazole is used against the major species of round worms, flukes and tape worms from animals and humans (20,21). They are commonly used to control infections and are extensively bound to plasma proteins in treated animals. Residues reduce the concern to the consumer that might result from persisting in meat. Therefore, residues of anthelminthic compounds can be found in meat products, so it is necessary to consider the withdrawal periods after therapy.

### 3.2. Antibiotics and other antibacterial compounds

Antibiotics and other antibacterial compounds are widely used for therapeutic reasons in short courses of treatment to control diseases in food animals and are also used at low levels for growth promoting purposes (11,12,17,22,23). The antimicrobials which are commonly used in food for animals can be classified to five major groups, including beta-lactams (e.g, penicillins and cephalosporins), tetracyclines (e.g., oxytetracycline, tetracycline and chlortetracycline), amino glycosides (e.g., streptomycine, neomycin and gentamycin), macrolides (e.g., erythromycin) and sulfanomides (e.g., sulfamethazines) (17,24). The relative occurrence of antimicrobial drugs in animal tissue varies widely which depends on the compound and the method of administration (11,12,17,25). The sulfonamides have the greatest residue problems, especially in swine. Aminoglycoside and tetracycline antibiotics are also relatively stable in animal tissues.

Others like the beta lactam group may vary widely depending on the formulation, dosage, and administration route (12). Low levels usage in feeds as growth promotors less likely results in considerable residues than therapeutic use. We should be avoided to use antimicrobial residues in meat products for several reasons: a) some residues can cause idiosyncratic reactions in ultra-sensitive consumers which could be extremely serious, b) residues are illegal generally, c) residues are indicative that the meat products may have come from animals that have a serious infection and d) the use of antibiotics in livestock species may result in antibiotic-resistant strains of microbial pathogens, potentially complicating treatment for both animals and humans.

### 3.3. Anabolic agents

Natural and synthetic anabolic agents have been administered to livestock to improve feed efficiency. Other types of drugs have also been used to reduce the ratio of fat to lean such as beta- agonists (e.g., clenbuterol) and some tranqulizers such as diazpam. Animal trissues contain low levels off naturally occuring anabolic streoids (12,23,26). The main biologically active steroids are progestrone, testosterone, 17- beta-estradiol and estrone (27). Steroid hormones, are given to animals to improve their rate of weight gain and feed efficiency. The most likely explanation of this effect is that pituitary is stimulated to produce increased quantities of growth hormone (10, 28). Some synthetic anabolic agents such as diethylstibestrol (DES) have been banned in the United States because of carcinogenic potential effects. The Euroupean Economic Community (EEC) has banned use of anabolic agents and beta agonists. There is, however, evidence of widespread illegal use in the EEC. Use of growth hormones (somatotropins) has been very controversial but does not appear to result in tissue residues above those naturally present (12). Although it has been concluded that beef raised with hormonal supplements has no adverse effect on humans and they are safe for cows and humans (29,30) the World Trade Organization (WTO) has partially accepted European Union (EU) contentions for prohibiting the use of growth-promoting hormones in cattle (31).

## 4. Effect of processing

Lipid in meat is a susceptible compound during storage and processing. Oxidation of lipid can occur in foods with high fat content and high-grade unsaturated faty acids. Adverse effects can be off-flavors, typical rancidity, and formation of toxic aldehydes. The balance between antioxidant and oxidizing agents and the loss of nutritional quality because of polyunsaturated fatty acid (PUFA) degradation impact on oxidative stability of fatty food. Sea food like shrimp has an amount of considerable fat, so susceptible to lipid oxidation (32).

Toxic chemical compounds may form during Maillard reaction like Furan. It is a strong hepatotoxin and hepatocarcinogen chemical in rodents which is classified as a group 2B, i.e. probably carcinogenic to humans according to IARC. It has been found in a wide range of foods such as canned foods, fish and fish oil with thermal processing like cooking, roasting, baking, pasteurization, and sterilization. The most important constituents as precursors for furan production are ascorbic acid, amino acids, carbohydrates, unsaturated fatty acids, and carotenoids. Ascorbic acid has the highest potential to produce furan. Accumulation of furan can be a result of food heating process in closed systems, such as jars and cans. Major way to reduce the content of furan in foods is optimizing the thermal condition, time, pH and discounting the precursor levels (33).

Ordinary cooking procedures may result in degradation of a number of antibacterial drug residues, which depends on the heat treatment duration. The time and temperature used in cooking are two main parameters affecting on antibiotic residues, where sufficient heating temperature and time can reduce several antibacterial drug residues (34).

Tilmicosin as a macrolide antibiotic, was reduced by boiling and microwave significantly. In the boiling method, tilmicosin reduction was higher over time; however, it was inversely related to tilmicosin initial concentration. A significant and positive correlation between sample central temperature and tilmicosin reduction was observed. In the microwave method, tilmicosin reduction was not affected by time or tilmicosin concentration. The surveillance data from tilmicosin concentrations in raw tissue like meat are not completely applicable for consumer exposure and dietary intake calculations, while the product is consumed in whole cooked (35).

The effect of frying on tylosin residue in minced meat was evaluated. Tylosin reduction percent, weight reduction percent of samples and their center temperature were defined after frying. In all treatments, tylosin in fried samples was significantly less than raw samples ($p<0.05$). Tylosin reduction (%) amount showed a significant and positive correlation with sample weight percent, sample center

temperature and frying time. Increasing frying time resulted in higher rate of tylosin, sample weight decrease, while sample center temperature increased (36).

## 5. Public health concerns

An important concern of chemical contaminants and residues in meat products is the possible transmission of harmful compounds from these products to human. Antibiotics used as feed additives are one the major concerns. They include tetracycline, nitrofurane, and sulfonamide (9). Biologically active metabolites of antimicrobial in meat products could result in anaphylaxis and allergic shock in sensitized individuals (e.g., penicillin, or adding chemical materials in meat products such as sodium nicotinate and sodium sulfite) (11,12). Overuse of antimicrobial in agriculture production causes toxicity such as aplasia of the bone marrow (e.g., chloramphenicol) (12,17,37), carcinogenic effects (e.g., oxytetracycline and furazolidone), and react with nitrite to yield (carcinogenic) nitrosamines (e.g., oxytetracycline) (9), effects on the human gut microflora populations (38), the emergence of resistant bacteria within animals and the transfer of antibiotic resistance genes (R-factor) from non-pathogenic bacteria to other bacteria or human pathogens which will cause resistance (2,9,37). Antimicrobial residues such as sulfonamide drugs can remain active in frozen or cooked meats muscle for long times (39). Furthermore, cooking does not destroy anti-parasite residues such as oxfendazole in meat and meat products (40).

Chronic toxic effects of low levels of residues are of concern, since the acute level may kill the animal. Neurotoxicity of heavy metals such as lead and mercury is an example of chronic toxicity (12).

Residue of hormones in meat are mostly the first concern of consumers (compared to other health related issues like saturated fatty acids, cholesterol) in Europe and North America (41). In Germany, 76-83% of men and 70-87% of women consider hormones in meat at high or very high risk (42). That is important because hormone residues can cause incidence of cystic ovarian disease in women (43) and beta-adrenergic receptor agonists are growth-promoting drugs with the potential for illegal use in livestock, and human toxicity has resulted from consumption of contaminated meat (44).

There is also concern about mycotoxins such as aflatoxins (the possible hepatotoxicity as well as mutagenicity and carcinogenicity) (9,45) and (the possible nephropathy and teratogenic effects) (9).

## 6. Conclusion

As the population of the world continue to grow, animal production will need to become more efficient, and may be accompanied by increasing demands for drug treatment, to better use of pesticides, hormones, antimicrobials, anti-parasite drugs, feed additives, food additives, and to reduce chemical materials in meat products. So, chemical contaminants can occur at every step of production from raw materials to consumer. They can directly enter to meat products by humans or indirectly enter from environment and food chain. Some chemical contaminants may be harmless at the low range of occurrence, and others are hazardous because they can cause toxic risks for human consumers such as tranquilizers, beta-agonists, and hormones. Therefore, continued monitoring and periodic reassessment of risks posed by these contaminants is needed to detect or anticipate new problems so that appropriate action can be taken in the interest of public safety. The use of food safety and quality assurance in farms and plants is very important to reduce chemical contaminants in meat and meat products. Any chemical or drug used in the breeding of livestock or poultry must meet several criteria:

1) They must be effective at the proposed dosage level for the proposed use.
2) The drug or chemical must not leave a residue in the edible tissues of the animal or poultry that is at a level which is judged harmful to the consumer.
3) The use of drug or agricultural compound must serve useful purpose in the production of the feed crop, animal or poultry.
4) An analytical detection method must be available which is capable of detecting the substance at or below the tolerance level.
5) The chemical and drug compounds must be used in a manner that would not contaminate their environment or the food supply.

## Conflict of interest

The authors declare that they have no conflict of interest.

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