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Toxicological issues associated with production and processing of meat

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ABSTRACT

Meat is a very complex and continuously changing *ex vivo* system of various high- and low-molecular substances that can be used for satisfying needs of the human organism for metabolic energy, building material and fulfilling of the other vital functions. A great majority of these substances are useful and safe for the consumer. Yet, meat and meat products may always contain substances exerting detrimental effects to the consumer's organism. The present paper is a literature review of the most important potentially toxic substances found in meat and meat products; their classification, ways of getting into the meat or formation during meat processing, undesirable physiological outcomes and biochemical mechanisms of their toxic effects, and methods for reduction of these responses.

1. Introduction

Meat as the flesh of animals used for food is a relevant dietary source of proteins, essential amino acids, chemical elements (e.g. iron, zinc) and vitamins (e.g. B_{12}, D). Yet, the healthy image of meat is tarnished by its negative association with saturated fat and cholesterol, and with non-nutritional issues like the presence of various toxic contaminants, including the most commonly found persistent organic pollutants or POPs (dioxins, polychlorinated biphenyls (PCBs)); polyaromatic hydrocarbons (PAH) in smoked products, heteroaromatic amines (HAA) in cooked products, and leukotoxin diols in comminuted meat products. A number of other potentially toxic compounds are also possible to identify and quantify in meat and meat products. Certainly, the actual toxicity of any compound depends on the dose and period of contact with the organism, on the other components of the food as well as on the individual characteristics of the human or animal host.

Meat and offal, especially liver and kidneys, can carry over from plants and concentrate the toxicants of environmental and plant origin and their metabolites. Processing of meat may lose or reduce the concentration of some substances and ibid create new, including toxic ones.

Meat toxicants can be divided by their origin as:

1. Geochemical pollutants from soil, such as arsenic.
2. Mostly anthropogenic environmental pollutants, such as lead, PCBs, or pesticide residues.
3. Toxic metabolites of microorganisms, such as mycotoxins inhabitating feed plants.
4. Endogenous plant toxicants, such as ptaquilosides.
5. Animal endogenous poisons, such as phytanic acid.
6. Veterinary drug residues.
7. Toxicants, borne in meat during processing and storage, such as PAHs, botulinum toxin, or biogenic amines.

Substances, belonging to the first six groups enter the meat production chain during breeding of the meat-producing animals, the seventh group during meat processing and storage. Since toxic substances may enter this chain, extending from "field to fork" at different points, a comprehensive risk assessment of potentially toxic substances in meat and other animal-derived products must be performed throughout the chain starting with the assessment of the fodder. The incidences of chemical contamination of chicken meat are largely confined to the primary production level. Contamination can result from deliberately added chemicals, such as pharmaceuticals and feed additives, or from environmental contaminants, such as mycotoxins or dioxins. The risk assessment of potentially toxic substances in feed requires a multidisciplinary approach, combining feed technology, animal nutrition and toxicology. A special aspect of this assessment is the consideration of potential accumulation and carry-over of substances within the food chain and their possible contribution to the overall human exposure via food of animal origin. Indeed, such an integration of feed and food in one risk assessment process is part of the mandate of the General Food Law (178/2002/EC) and methodologies have evolved considerably over the past ten years (Dorne & Fink-Gremmels, in press).

In Europe, undesirable substances are regulated by the Directive 2002/32/EC of the European Parliament and of the Council (EC) that provides the possibility to establish maximum levels for specific substances in animal feeds with the aim to protect animal health, public health and the environment (EC, 2002a). Over the past 10 years, the Panel on Contaminants in the Food Chain (CONTAM) of the European Food Safety Authority (EFSA) has developed a standardized and transparent procedure for the risk assessment of contaminants in feed and food. CONTAM has published over 30 scientific opinions addressing specific feed contaminants and groups of contaminants, such as heavy

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metals and metalloids, POP, mycotoxins, natural plant toxins, such as glucosinolates, saponins, cyanogenic glycosides (Dorne et al., in press).

2. Overview of adverse physiological effects and main toxicity mechanisms connected with consumption of meat and meat products

Toxicology divides the exposures and adverse responses into acute, subchronic, and chronic ones. An acute response follows an acute exposure and develops quickly, usually with severe symptoms. Symptoms of chronic intoxication emerge slowly as a response to a systematic repeated long-term exposure to relatively smaller doses of the toxicant. Acute poisonings with meat products are nowadays rare, and if they even happen, then mostly, like botulism, are driven by microorganisms. Chronic toxic effects of many substances are systemic involving a number of physiological alterations in multiple organs or tissues (Table 1).

Gradually extending life spans lead to increased morbidity and mortality numbers from chronic, lifestyle, including diet-influenced, diseases. Therefore, cancer development has become the most important and, hence, most studied chronic toxic response exerted by a majority of the toxicants listed in Table 1. There are two types of carcinogenicity mechanisms: 1. genotoxic or DNA-reactive, including a direct interaction between a carcinogen (also mutagen) and DNA, and 2. epigenetic, directly not involving DNA. In addition, a number of carcinogens act by a still unspecified way. For example, the mechanism of carcinogenicity of ochratoxin is still not fully established and the existence of several substantially differing mechanisms is not excluded (Pföhl-Leszkowicz & Manderville, 2012). The first type of carcinogens, in turn, can be divided into activation independent (primary) and activation dependent (secondary) carcinogens and a heterogenous group with the common name inorganic compounds. Most of the meat-borne carcinogens, such as PAHs, HAA, aflatoxins, ptaquiloside and nitroso-compounds, are secondary carcinogens. Directly DNA-reactive carcinogens are considered to be of higher concern because they do not demonstrate a dose below which they are not carcinogenic. Any single exposure to these compounds is associated with a definite risk of producing a carcinogenic effect proportional to the dose. The response to their toxic effect of these substances may appear already after a very first random contact and the response is cumulative.

The toxicity of a number of substances can be explained by the receptor-mediated mechanisms at the plasma membrane or cytosolic level. The key receptor, involved in the transfer of the adverse signals is the cytosolic aryl-hydrocarbon receptor (AhR) that is one of the main factors of the ligand-activated transcription or RNA-synthesis and synthesis of essential proteins. AhR also activates a gene battery connected with phases I and II of xenobiotic metabolism. The agonists of AhR are hydrophobic aromatic planar molecules, such as PCBs, and PAHs. Neurotoxic effects of cyclodiene-type insecticides like dieldrine or heptachlor are conveyed by antagonistic interactions with membraneous γ-aminobutyric acid (GABA) receptors.

A frequent group of adverse physiological effects is endocrine disruption (Table 1). Endocrine disruptor (ED) is an exogenous substance or a mixture that alters the functioning of the endocrine or hormonal system of the body, causing adverse health effects on an intact organism, its progeny or (sub)populations. EDs interfere with the organisms' ability to regulate growth, development, metabolism or other functions. There are hundreds of EDs, mostly anthropogenic, in the environment, in food, and in consumer products that can contribute to a wide range of diseases and disabilities. Several mechanisms of endocrine disruption can be explained with binding of ED to various estrogen receptors or other receptors, or receptor-free processes.

EDs are classified as follows: I. Compounds with a strong evidence of ED activity and with a high level of exposure probability. II. Potential EDs or compounds with a medium level of concern with regard to exposure and III. Compounds with an insufficient evidence of ED activity, or with a low level of concern with regard to exposure. Concerning meat and meat products, group I is represented by bisphenol A (BPA), several PCBs, dioxins 1,2,3,7,8-PCDD and 2,3,7,8-TCDD and furans (2,3,4,7,8-PCDF), organochlorine pesticides such as dichlorodiphenyltrichloroethane (DDT), chlordane, lindane and others, and herbicides such as acetochlor, alachlor, or atrazine (Mezcua et al., 2012). Very often, especially in the case of toxicants belonging to the group III, the decision whether to allow consumption of the respectively contaminated matrix or not is made on the basis of risk and benefit evaluation.

Table 1
Characterization of toxic responses connected with consumption of meat products.

Toxicant	Main adverse physiological outcomes	Main biochemical mechanisms
Arsenic	Carcinogenicity (unclassified), neurotoxicity, cardiovascular toxicity, diabetes	Oxidative stress (glutathione), multiple other mechanisms
Cadmium	Carcinogenicity (both types), acute pulmonary and renal toxicities and testicular damage, osteomalacia	Oxidative stress; reduction of bloodflow, disturbance of Ca metabolism, inhibition of DNA repair
Lead	Neurotoxicity, GIT toxicity, hematopoiesis toxicity (anemia), nefrotoxicity	Enzyme inhibition via binding to SH-groups; replacing of Zn
PCBs	Neurotoxicity, immunotoxicity, anemia, atherogenicity amplified by leukotoxin (LTX)	Endocrine disruption via cytosolic AhR
Dioxins	Carcinogenicity (epigenetic), teratogenicity, immunodepression via thymus damage, reproductive toxicity	Endocrine disruption via cytosolic AhR
Aflatoxins	Carcinogenicity (genotoxic), mutagenicity, teratogenicity, acute and subchronic toxicity with various symptoms	Conjugation with guanidine base in DNA
Ochratoxins	Nephrotoxicity, teratogenicity, renal carcinogenicity (genotoxic?), neurotoxicity	Reduced glyconeogenesis and anion transport leading to intercellular alkalinization;
Ptaquiloside	Carcinogenicity (genotoxic)	Alkylating of adenine in DNA
Phytanic acid	Carcinogenicity (non-Hodgkin lymphoma), immunodepression via thymus damage, reproductive toxicity, teratogenicity	Oxidative stress; cell proliferation through receptor (PPAR)-α, etc.
Organochlorine pesticides (DDT)	Carcinogenicity (rodents), reproductive toxicity?, neurotoxicity	Endocrine disruption via androgen receptor; closing of Na-channels
Leukotoxins (LTX and especially LTXD)	Carcinogenicity, mutagenicity, cardiotoxicity (induction of endothelial dysfunction, amplifying of atherogenic effect of PCBs)	Endocrine disruption, cytotoxicity
PAHs	Carcinogenicity (genotoxic), mutagenicity, hepatotoxicity, immunotoxicity, GIT toxicity	Mutagenicity via DNA attack
HAAs	Carcinogenicity (various organs), mutagenicity	Via interaction with AhR
Biogenic amines	Acute cardiovascular toxicity via pathological broadening of peripheral blood vessels	Reduction of amine metabolism, primarily of histidine
Botulinum toxin	Acute neurotoxicity	Muscle paralysis via inhibition of acetylcholine release
Bisphenol A	Genotoxicity, low dose effect	Endocrine disruption without classical estrogen receptor
Phthalates	Reproductive toxicity, hepatotoxicity, incl. hepatocarcinogenicity	Endocrine disruption via receptor
Nitrites	Activation dependent rodent carcinogenicity, no human effect approved; anoxia	Nitrosamines as main active particles; oxidation of hemoglobin

Abbreviations: GIT — gastrointestinal tract; LTX — leukotoxin; LTXD —leukotoxin-diol; PCB — polychlorinated biphenyls; PAH — polyaromatic hydrocarbons; HAA — heteroaromatic amines; AhR-arylhydrocarbon receptor; PPAR — peroxisome proliferator-activated receptor.