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Food Safety Concerns of Pesticides, Veterinary Drug Residues and Mycotoxins in Meat and Meat Products

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Abstract: The aim of this review was to focus on food safety in relation to pesticide and veterinary drug residues and mycotoxins in meat and meat products. The impact of these consumers awareness is a large concern for the meat industry. In order to be more prepared, the consumer strive to have more complete information on the sources of inputs in their products, because consumers are becoming more worried about this. Residues in meat and their products are generally classified as naturally present, caused by man and arise secondarily. In the past, most contamination of meat resulted from natural toxicants. However, usage of synthetic chemicals for regular house-hold and agricultural practices while benefiting society has also provided new sources of potential contamination. The levels of pesticide residues are now over alarming situation in certain countries. Drug residues in meat are relatively uncommon whereas, aflatoxin or ochratoxin are rarely found. Residues from secondary residues also occur less frequently. This study reviews the causes of residues in meat, types of residues found, their detection methods, incidences and their regulation with emphasis on public health risk and their assessment.

Key words: Meat safety, pesticides, veterinary drugs, mycotoxins, residues

INTRODUCTION

Residues in the widest sense may be defined as undesirable substances present in meat. These substances are chemical or biological in nature and have always been present in a small amount or can be introduced into the environment by various technological practices, can arise as a result of incorrect storage of food stuff, can get in to the food chain due to modern agricultural practices and thus introduced into the foods or they may be results of medicines given to the animals or of processing methods.

Surveillance/monitoring on the occurrence of residues in meat and their products were relatively a neglected area until last decade. But with the advancement of technological intervention regarding livestock rearing, disease control and intensive crop production system, the chances of residues in foods of animal origin increased tremendously. This results a potential risk of various life threatening diseases such as cancer, leukemia,

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reproductive disorder besides disruption of body's immune, endocrine and nervous system (van Wendel de Joode *et al*., 2001; Horrigan *et al*., 2002). The growing awareness of public perception about this reduces the confidence among the consumers and resultant adverse impact on global economy. Ideally, meat food should be completely free from such types of contaminants. This is a utopian goal considering current agricultural and technological practices. Many develop countries in the world have already been tracking this problem by fixing statutory limitations of pesticides, veterinary drug residues and microbial toxins in meat and meat products and their enforcement through monitoring to ensure safe food supply to consumers. Monitoring of such types residues in foods of animal origin can reveal current status of contamination, thus enabling preventive and control measures to be initiated before contamination becomes so serious or wide spread that threatens human health or causes serious economic losses.

Source of Exposure

Pesticides have unique status of all food residues because these compounds are regularly used in agricultural fields to meet worldwide food demands. It is estimated that, without pesticides, world production of food would be reduced by 30%. Despite the obvious benefits, however, occasional misuse of such chemicals has resulted in intoxication of animals and/or accumulation of residues in meat, poultry and meat products. Among all pesticides, organochlorine (OC) compounds such as DDT, lindane or hexachlorobenzene, heptachlor, heptachlor epoxide, aldrin/dieldrin are mostly persistent in the environment and cause major health hazard effects. Some of these compounds such as mercury, arsenic etc. also contain toxic elements which, when break down in the soil, produce the actual residues. The industrial chemicals (chlorinated hydrocarbons) such as PCB, the dioxin, or perchlorethylene (PER) play the main parts, but organometal compounds such as tetraethyl lead in fuel, benzopyrene and other substances are also important (Table 1).

In contrast to pesticides, residues of veterinary medicinal products are most common in foods of animal origin as are directly exposed to the animals (Table 2). But this could be avoided, if used properly with sufficient withdrawal period of times. Drug residues in meat occur, when these are used via parental or oral route or as feed additives in food animals. The range of veterinary medicinal products used in regular animal husbandry practices is extremely wide, ranging from teat dips to hormones. Approximately, 42% of all veterinary

Table 1: Maximum Residue Limits (MRLs) of pesticides (ppm) in meat

	PFA rules	Codex standards	U.S
Pesticide standard	Meat and poultry	Cattle meat	Cattle meat
Aldrin/dieldrin	0.2	0.2	0.3 (fat)
Chlordane	-	0.05	0.3 (fat)
Aldicarb	-	0.10	0.01
Carbaryl	-	0.10	0.10
Chlorpyrifos	0.1	2.0	0.2
Cypermethrin	0.2	0.02	0.05
DDT and its metabolites	7.0 (fat)	5.0 (fat)	5.0 (fat)
Decamethrin/deltamethrin	-	0.03	-
Endosulfan	-	0.10	0.2
Fenvalerate	1.0	1.5	1.5
Heptachlor	0.15	0.2	0.2
Hexachlorobenzene	0.2	0.2	0.5
Lindane	2.0	1.0	7.0
Monocrotofos	0.02	0.02	-
Propoxur	-	0.05	-

-: Data not available, Source: MOHFW (2004)

Table 2: Codex Maximum Residues Limit (MRLs) and Acceptable Daily Intake (ADI) levels of some important antimicrobial drugs in food of animal origin

Antimicrobial	Acceptable daily intake (ppb)	Target tissue (ppm)			
		Muscle	Liver	Kidney	Fat
Ampicillin	-	0.050	0.050	0.050	0.050
Benzyl/Procaine benzyl penicillin	0-30	0.050	0.050	0.050	0.050
Cloxacillin	-	0.300	0.300	0.300	0.300
Erythromycin	-	0.400	0.400	0.400	0.400
Gentamicin	0-20	0.100	0.200	0.500	0.100
Sulfadimidine	0-50	0.100	0.100	0.100	0.100
Sulfonamides (combinations)	0-50	0.100	0.100	0.100	0.100
Streptomycin	0-50	0.600	0.600	0.100	0.600
Oxytetracycline	0-30	0.100	0.100	0.100	0.100
Tetracyclines (OTC+CTC+TC)	0-30	0.100	0.100	0.100	0.100
Trimethoprim	-	0.050	0.050	0.050	0.050

Data not available

pharmaceuticals used world-wide are used as feed additives, 19% are used as anti-infectives, 13% as parasiticides, 11% are used as biologicals and 15% represent other pharmaceuticals. All of them are administered to animals either by injections (intramuscularly, intravenous, subcutaneous) or orally in the feed and water, topically on the skin and by intra-mammary and intra-uterine infusions (Mitchell *et al*., 1998). Injectables were responsible for 46% of the violative residues in meat followed by oral administration at 20% (feed, water and bolus) and intra-mammary infusions at 7%. Several other factors have contributed to the residues problem such as poor treatment records or failure to identify the animals and result from the use of a drug in same manner that is inconsistent with the labeling. This occurs primarily through not observing label of withdrawal times as well as extra-label use of drugs.

The microbial residues mostly mycotoxins, metabolites of toxigenic molds (fungi) are present in feedstuffs. During the course of evolution organisms have accustomed themselves to certain toxic contents in foods. However, the direct consumption of mycotoxin-contaminated cereal grains is much more probable than exposure to residues in foods of animal origin because livestock and poultry have the ability to dilute or detoxify these chemicals (Michael and Buck, 1987; Van Zytveld *et al*., 1970; Sims *et al*., 1970).

Detection of Residues in Meat and Meat Products

Pesticides

Conventional Methods

A number of analytical techniques such as colorimetric method, Thin Layer Chromatography (TLC), High Performance-Thin Layer Chromatography (HP-TLC), Gas Liquid Chromatography (GLC), Gas Chromatography-Mass Spectrometry (GC-MS), High Performance Liquid Chromatography (HPLC), Liquid Chromatography-Mass Spectrometry-Mass Photometry (LC-MS-MS) etc., are established for detection and quantification of pesticide residues in animal tissues (Argauer *et al*., 1995; Bogialli *et al*., 2003; Pecorelli *et al*., 2004). However, colorimetric and TLC method are limited only for qualitative determination due to its low sensitivity. GLC or GC-MS though normally used for determination of non-volatile compounds (organochlorine and organophosphorus pesticides), but also effectively utilized for determination of thermo-labile compounds such as synthetic pyrethroid and N-methyl carbamate pesticides.

Modern Methods

Although, conventional techniques such HPLC/MS and GC/MS gives satisfactory analytical results for pesticide determination, new assays and sensors for cheaper and faster on-site analysis are being developed. Enzymatic sensors, based on the inhibition of a selected enzyme, are the most extended biosensors used for the determination of these compounds (Choi *et al*., 2001; Andres and Narayanaswamy, 1997). Biosensors based on enzyme inhibition although sensitive, are not selective and cannot, therefore, be used for quantification of either an individual or a class of pesticides. But introduction of recombinant enzyme for biosensor applications can solve the problem. The organophosphorus hydrolase (OPH) is able to hydrolyze a number of OP pesticides such as paraoxon and parathion and chemical warfare agents such as sarin and soman. Hydrolysis of these OP pesticides generates p-nitrophenol, which is an electroactive and chromophoric product. Thus, OPH could be combined with an optical transducer to measure the absorbance of p-nitrophenol or with an amperometric transducer to monitor the oxidation or reduction current of this product (Mulchandani *et al*., 2001). In a different approach, biosensors based on immunological assays have been developed with limit of detection of 0.1 $\mu g\ L^{-1}$. Mallat *et al*. (2001) applied the River Analyzer (RIANA) immunosensor in the determination of pesticides such as atrazine, simazine, isoproturon, 2,4-D, alachlor and paraquat in natural waters. Recently, a label-free direct piezoelectric immunosensor built on a flow-through cell was used for the determination of 2, 4-D in water with a limit of detection around 0.2 $\mu g\ L^{-1}$. However, there are very limited applications of biosensor detection of pesticide compounds in meat system.

Veterinary Drugs

Conventional Methods

For determination of veterinary drug residues in foods, currently, 6 types of detection methods are commonly used. These include microbial growth inhibition assays, microbial receptor assays, enzymatic colorimetric assays, receptor binding assays, chromatographic methods and immunoassays. But microbial growth inhibition assays and later 2 methods are popular for monitoring of antimicrobial residues in meat and meat products as are capable of detecting a broad range of these drugs (Mitchell *et al*., 1998; Biswas *et al*., 2007). Korsrud *et al*. (1998) evaluated a number of common bacterial inhibition test for screening antimicrobial drug residues in tissues. They found that screening for tetracycline was excellent with German three-plate test, the European Union four-plate test and new Dutch kidney test instead of Swab Test On Premises (STOP), Calf Antibiotic and Sulfa Test (CAST) and the Fast Antibiotic Screen Test (FAST).

Modern Methods

Most of the biosensors developed are aimed at determining them in biological or food samples. The Surface Plasmon Resonance (SPR) technique has been developed and demonstrated for on-line/at-line detection of veterinary drug residues in milk, porcine bile and bovine urine, including a commercial handling robot. This sensor operates in real time and it may detect up to 8 different veterinary drugs simultaneously with a throughput of up to 600 samples day^{-1}. The SPR techniques are having a major impact on the development of new optical biosensors. Sulfamethazine has been determined by Akkoyun *et al*. (2000) with an optical immunosensor in animal urine. Hansen and Sorensen (2000) presented three different reporters gene systems from *V. fischeri*, *E. coli* and *Aequorea victoria* all combined with a tetracycline inducible promoter in the development of three corresponding whole-cell biosensors. They respond to low levels of tetracyclines by producing galactosidase, light

or green fluorescent protein, respectively. In the field of food monitoring, different biosensors were able to determine penicillin G (Setford *et al*., 1999) or tetracyclines (Hansen and Sorensen, 2000), both in milk.

Mycotoxins

Conventional and Modern Methods

The TLC and HP-TLC is regularly used for determination of micotoxins in foods. However, a great number of specific sensors for bacterial toxins and mycotoxins have been developed for food and environmental control (Delehanty and Ligler, 2002). Thus, an integrated optical sensor has been reported for the analysis of aflatoxin B in corn. A light-addressable potentiometric immunosensor based on the commercial device for the analysis of saxitoxin and ricin has also been described. An impedance-based immunosensor has been prepared by using an ultrathin platinum film with an immobilized layer of antibodies against the staphylococcal enterotoxin B (Kumar *et al*., 1994). Various evanescent wave immunosensors have also been reported to be capable of detecting botulin with very low limits of detection. A rapid and sensitive immunosensor for the detection of the Clostridium botulinum toxin A has also been developed. This fiber optic-based biosensor utilizes the evanescent wave of a tapered optical fiber where antibodies antitoxin A has been covalently immobilized at the distal end. The toxin could be detected by means of a rhodamine label, within a minute at concentrations as low as 5 ng mL^{-1}.

Residues and Health Risk

Among all residues, pesticides receiving most interest worldwide in recent years. Though violative level of pesticides are relatively uncommon, a low violation rate even remain an important public health consideration because of their wide spread use in meat and poultry production, their persistence in environment and varying toxicity. The United Nations has estimated that about 2 million poisoning and 10, 000 deaths occur each year from pesticides, with about three-fourth of this occurring in developing countries. The acute and malicious consumption involving higher dose results in death whereas, chronic insidious intake lead to elevated cancer risk and disruption of body's reproductive, immune, endocrine and nervous system (Horrigan *et al*., 2002).

The carcinogenicity of organochlorine (OC) pesticides has been studied in a number of laboratory animals including non-human primates. Lifetime or limited period of time treatment of mice with DDT induced liver tumors including malignant metastasizing hepatoblastomas. DDT also increased incidences lung tumors and lymphoma in mice, liver tumors in rats and adrenal adenomas in hamster. However, DDT did not induce DNA damage in bacteria or cultured rodent and human cells. It induced chromosomal aberration in mouse but not in rat bone marrow cells. DDT and its metabolites inhibited gap-junctional intracellular communication.

Other areas of concerns are childhood brain cancer and cancers of nervous system. Studies suggest an increase in risk in brain cancer, leukemia, Wilm's tumors, Ewing's sarcoma and germ cell tumors associated with paternal occupational exposure to pesticides prior to and during pregnancy. However, maternal occupational exposure during pregnancy was less frequent but was also associated leukemia, Wilm's tumors and germ cell tumors. Pesticides can suppress immune system, as epidemiological evidence shows an association between pesticide exposure and increase incidence of human disease, particularly those disease to which immuno-compromised individuals are especially prone. The endocrine disrupter includes atrazine and alachlor. However, there is strong need of sufficient data for complete health hazard evaluation in this context.

In contrast to pesticides, exposure from veterinary drug residues rather most common as are directly injected or fed to the animals. The overuse of antimicrobials such as tetracyclines, sulfonamides, amino glycosides, β-lactam derivatives etc. in animal production or their residues in food system pose potential allergic reactions in sensitized individuals, but sub therapeutic and therapeutic levels may perturb human gut micro flora (Paige *et al*., 1997). The tetracyclines are incompletely absorbed from the gastrointestinal tract; they reach readily high concentrations in the intestine, producing perturbations of the intestinal microflora within 48 h of daily treatment. Experience with tetracyclines in human medicine indicates that therapeutic levels of tetracyclines can perturb the intestinal microflora by inducing emergence of resistant strains and altering the metabolic activity of the microflora, its resistance to colonization by pathogenic, opportunistic or resistant microorganism barrier effect and its ecological balance, without any identified deleterious effect. Immunodepression and phototoxicity may also occur in animals and human beings besides superinfections related to tetracyclines. Treatment with oxytetracycline during the second month of pregnancy presents a teratogenic risk to the foetus (Czeizel *et al*., 1998; Czeizel and Rockenbauer, 2000). As an undesirable side effect, OTC not only discolours the primary and permanent teeth but also causes hypoplasia in developing teeth when administered to the infants, mothers during last two trimesters of pregnancy and children under 12 years of age. However, unwanted risk is highest when OTC is given to neonates and babies prior to the first dentition (Tanase *et al*., 1998). Sulfonamides (sulfadimidine and sulfamethoxazole) can induce thyroid, adenoma and hyperplasia in laboratory animals. It has also potential carcinogenic character. To reduce bacteria resistance to sulfonamides to get synergistic effect, pyrimethamines such as trimethoprim and oriprim are used in combination.

The National Research Council and Institute of Medicine have noted a link between the use of antibiotics in food animals and the development of bacterial resistance to these drugs causing human diseases. Similarly, scientist at Center for Disease Control and Prevention (CDC) began tracking a new type of *Salmonella* called Newport 9+ which is resistant to nine antibiotics including ceftriaxone, one of the few drugs that kill most bacteria and the drug of choice for children when *Salmonella* enter the blood stream. Nonetheless, toxicity of these antimicrobial chemicals includes aplasia of bone marrow, the emergence of resistant bacteria within animals and the transfer of antibiotic resistance gene to human pathogens. The appearance of resistance among pathogenic organisms such as *Salmonella* DT-104 and *Campylobacter* is of more concern (Glynn *et al*., 1998). *E. coli* is an opportunist pathogen capable of infecting people via the food chain and causing enteric infections in young children and travelers as well as range of other infections. Enteric infections with *Salmonella*, *E. coli* or *Campylobacter* rarely warrant antibiotic treatment and so one might argue that the problem is not nearly as important as Methicillin Resistant *Staphylococcus aureus* (MRSA) or other major human resistance problems. However, treatment failure has been reported (Smith *et al*., 1999; Fey *et al*., 2000) and the livestock industries can not ignore the problem. Enterococci have only been thought of as food borne organisms since discovery of Vancomycin Resistant Enterococci (VRE) in pigs and poultry and there is some dispute that their spread occurs from animals to people.

Similarly, uses of hormonal compound like DES in meat production known to have strong carcinogenic effects and are banned from use for food producing animals (Lee *et al*., 2001). On the other hand, beta-adrenergic agonist (clenbuterol, salbuterol, cimeterol) act through binding to receptor on target cells and act by repartitioning energy from fat to lean meat production. This compound in excessive amount leaves residues in meat and thereby adverse reaction in consumers requiring hospital treatment. Thus, health risks of veterinary

medicinal products and their metabolites are very difficult to define and their presence of above the violative level is illegal and subject to financial penalties in many countries (Paige *et al*., 1997).

The health implications from heavy metals lead to kidney damage, cardiovascular diseases, induction of hypertension, growth inhibition, interference in haeme synthesis, irreversible changes in brain and nerve cells and also some of these residues are known to be carcinogenic in nature. The pulmonary and nervous systems and skins are the main target organs of arsenic contamination. Cadmium associated with kidney damage and lead considered to has been associated with learning deficits in children. Copper and zinc are essential micronutrients but in higher amount may impact metallic taste to the product resulting unacceptability of the product.

Like other residues mycotoxin also mutagenic, carcinogenic, teratogenic or hepatotoxic to most experimental and domestic animals and man. Aflatoxin B_1 the most important mycotoxin in view of occurrence and toxicity, is a potential hepatocarcinogen in various species of laboratory animals tested, among which are fish, birds, rodents and monkey.

Regulation

In 1979, a US General Accounting Office (GAO) report identified 143 drugs and pesticides as likely to leave residues in raw meat and poultry. Of these, 42 are known to cause or are suspected to causing cancer, 20 are suspected teratogens and 6 are suspected mutagens (Shull and Chuke, 1983). In the ensuing 24 years these numbers have probably risen.

The regulation of residues handled by each country throughout the world has a tendency towards uniform approach. But much greater enforcement has been seen with the passage of WTO and sanitary and phytosanitary measures. In the United States, pesticide use is regulated under FIFRA (US, Federal Insecticide, Fungicide and Rodenticide Act) on the basis of risk-benefit standard. This balancing takes into account the economic, social and environmental cost as well as potential benefits of the use of any pesticide in relation to its efficacy, inherent toxicity to mammals, wild-life and plants. A given pesticide may have many different uses, but required individual approval by the U.S. Environmental Protection Agency (EPA) under FIFRA. In fact, in the United States, pesticide regulation is under auspices of three government agencies, the Environmental Protection Agency (EPA), the Food and Drug Administration and the United States Department of Agriculture-Food Safety Inspection Services (USDA-FSIS). The FDA and USDA-FSIS are responsible for monitoring pesticide residues in foods based on level set by the EPA. The FSIS is responsible for meat and poultry products and FDA covers all other types of raw commodities and processed food products. However, regulation of pesticides in European Union is done on the basis of their toxicological properties. The council directive of the European Economic Community 91/414/EEC specified criteria for plant protection products in relation to Acceptable Daily Intake (ADI) for man, Acceptable Operator Exposure Level (AOEL), acute reference dose and maximum admissible concentration in water. The international organizations such as Codex Alimentarius Commission (CAC) have also set their standards using the term Maximum Residue Limits (MRLs) and Acceptable Daily Intake (ADI) levels of various pesticide residues in meat and meat products.

In contrast to pesticides, the USDA-FSIS and the FDA are responsible for monitoring meat and poultry products for animal drug residues. The USDA-FSIS conducts the National Residue Programme (NRP) to prevent animals containing violative amounts of drug residues from market samples through extensive on-site sampling technique (FSIS-USDA, 1998). The

samples are also sent to FSIS field laboratories for further testing. The FDA Center for Veterinary Medicine (CVM) is responsible for approving new animal drugs, setting tolerances and enforcement action depends on results of FSIS findings (FSIS-USAD, 1999). Other international organizations include the European Agency for the evaluation of medicinal products (EMEA), Office International des Epizootics (OIE) and Consultation Mondiale de I' Industrie de la Sante Animale (COMISA). Many countries have specialist groups involved such as FDA in USA, the Bureau of Veterinary Drugs in Canada and the Veterinary Products Committee of Ministry of Agriculture, Fisheries and Foods in the United Kingdom. The essential parameters required for dietary exposure assessment at the national/international level are: (a) food consumption data, (b) food chemical data, (c) methods for estimating dietary exposure, (d) priority setting function of dietary exposure methods and (e) extent of over estimation, uncertainty and variability.

Statutory Limits/Risk Assessment of Residues

International Organization such as Codex Alimentarius Commission have taken initiation of harmonization of chemical residues in food through establishment of statutory limitations viz., Maximum Residue Limits (MRLs), Acceptable Daily Intake (ADI) levels, acute reference dose (ARfD), No Observed Adverse Effect Levels (NOAEL) etc. However all these statutory limitations are important principles for risk assessment of residues in foods including meat. For statutory limits of residues, the terms tolerances or Maximum Residue Limits (MRLs) are frequently used by regulatory agencies. But both the term tolerances and MRLs are synonymous; former is used in United States other countries, while later is used in Canada and the European Union. The term MRL may be defined as the maximum concentration of marker residue (e.g., parent compound, metabolites etc.), expressed in parts per million (ppm) or parts per billion (ppb) on fresh weight basis, that is legally permitted or recognized as acceptable in or on food. The MRLs are established on the basis of package of toxicology and residue data and these are referred to as safety file and the residue file. The toxicology data are used not only to characterize the biological properties of the molecules, but also to identify a suitable No Observed Effect Levels (NOELs), which in turn is used to calculate an Acceptable Daily Intake (ADI), the quantity, which if consumed over a human lifetime will have no adverse effect on consumer health. This in turn expressed on body weight basis and can be considered the safety standard for that compound. The MRL is then elaborated from this ADI along with knowledge of the depletion kinetics of the residues in the animal or its meat and with reference to standard intake values for particular types of food. The identification of NOELs, the calculation of ADI values and the establishment of MRLs is a complex scientific process involving toxicology, pharmacology, microbiology, residue kinetics and analytical chemistry but the MRL is established at a magnitude which ensures that the ADI will not be exceeded by the consumer when eating food of animal origin (Hartzell, 1996). Another Term Total Residue Levels (TRL) refers to the safe concentration of total residues that corresponds to the MRL.

The term Acceptable Operator Exposure Level (AOEL) and acute reference dose (ARfD) also practiced most commonly by European Union. The AOEL is defined as the maximum amount of active substance to which the operator may be exposed without any adverse health effect and is based on the highest level at which no adverse effect is observed in tests in the most sensitive relevance animal species. The AOEL is expressed as mg of chemical/kg body weight of the operator. On the other hand, the ARfD of a chemical is an estimate of the amount of substance in food or drinking water, expressed on the body weight basis, that can be ingested over a short period of time, usually during 1 meal or 1 day, without appreciable

health risk to the consumer, based on all the known fact at the time of evaluation. This calculated reference dose is compared to an estimate or measurement of exposure in the risk assessment process.

REFERENCES

Akkoyun, A., V.F. Kohen and U. Bilitewski, 2000. Detection of sulphamethazine with an optical biosensor and anti-idiotypic antibodies. Sens. Actuators B, 70: 12-18.

Andres, R.T. and R. Narayanaswamy, 1997. Fibre-optic pesticide biosensor basedon covalently immobilized acetylcholinesterase and thymol blue. Talanta, 44: 1335-1352.

Argauer, R.J., K.I. Eller, M.A. Ibrahim and R.J. Brown, 1995. Determining propoxur and other carbamates in meat using HPLC fluorescence and gas chromatography/ion trop mans spectrometry after supercritical fluid extraction. J. Agric. Food Chem., 43: 2774-2778.

Biswas, A.K., G.S. Rao, N. Kondaiah, A.S.R. Anjaneyulu and J.K. Malik, 2007. Simple multiresidue method for monitoring of trimethoprim and sulfonamide residues in buffalo meat by high performance liquid chromatography. J. Agric. Food Chem., 55: 8845-8850.

Bogialli, S., R. Curini, A.D. Corciad, M. Nazzari and M.L. Polci, 2003. Rapid confirmation assay for determining 12 sulfonamide antimicrobials in milk and eggs by matrix solid-phase dispersion and liquid chromatography mass spectrometry. J. Agric. Food Chem., 51: 4225-4232.

Choi, J.W., Y.K. Kim, I.H. Lee, J. Min and W.H. Lee, 2001. Optical organophosphorus biosensor consisting of acetylcholinesterase/viologen hetero Langmuir-Blodgett film. Biosensors Bioelectronics, 16: 937-943.

Czeizel, A.E., M. Rockenbauer and J. Olsen, 1998. Use of antibiotics during pregnancy. Eur. J. Obstetrics Gynaecol. Reprod. Biol., 81: 1-8.

Czeizel, A.E. and M. Rockenbauer, 2000. A population-based case-control teratologic study of oral OTC treatment during pregnancy. Eur. J. Obstetrics Gynaecol. Reprod. Biol., 88: 27-33.

Delehanty, J.B. and F.S. Ligler, 2002. A microarray immunoassays for simultaneous detection of proteins and bacteria. Anal. Chem., 74: 5681-5687.

FSIS-USDA, 1998. National Residue Program Report. USDA, Washington DC.

FSIS-USDA, 1999. The Impact of Pathogen Reduction/HACCP on Food Animal Production Systems. USDA, Washington DC.

Fey, P.D., T.J. Safranek, M.E. Rupp, E.F. Dunne and E. Ribot *et al*., 2000. Ceftriaxone-resistant salmonella infection acquired by a child from cattle. N. Engl. J. Med., 432: 1242-1249.

Glynn, M.K., C. Bopp, W. Dewitt, P. Dabney, M. Mokhtar and F.J. Angulo, 1998. Emergence of multidrug resistant *Salmonella enterica* serotype *typhimurium* DT104 infection in the United States. N. Engl. J. Med., 19: 1333-1338.

Hansen, L.H. and S.J. Sorensen, 2000. Detection and quantification of tetracyclines by whole cell biosensors. FEMS. Microbiol. Lett., 190: 273-278.

Hartzell, G.E., 1996. Overview of combustion toxicology. Toxicology, 115: 7-23.

Horrigan, L., S.L. Robert and P. Walker, 2002. How sustainable agriculture can address the environmental and human health harms of industrial agriculture. Environ. Health Perspect., 110: 445-456.

Korsrud, G.O., J.O. Boison, J.F. Nouws and J.D. MacNeil, 1998. Bacterial inhibition tests used to screen for antimicrobial veterinary drug residues in slaughtered animals. J. AOAC Int., 81: 21-24.

Kumar, P., J.T. Colston, J.P. Chambers, E.D. Rael and J.J. Valdes, 1994. Detection of botulinum toxin using an evanescent wave immunosensor. Biosens. Bioelectron., 9: 57-63.

Lee, M.H., H.J. Lee and P.D. Ryu, 2001. Public health risks: Chemical and antibiotic residues. Rev. Asi. Aust. J. Anim. Sci., 14: 402-413.

MOHFW., 2004. Contaminants in foods: Prevention of food adulterationContaminants in foods: Prevention of food adulteration Act 1954, (Ammendment 2004). Ministry of Health and Family Welfare.

Mallat, E., C. Barzen, R. Abuknesha, G. Gauglitz and D. Barcelo, 2001. Fast determination of paraquat residues in water by an optical immunosensor and validation using capillary electrophoresis-ultraviolet detection. Anal. Chim. Acta, 427: 165-171.

Michael, L.B. and W.W.B. Buck, 1987. Chemical contaminants: Their metabolisms and their residues. J. Food Prot., 50: 1058-1073.

Mitchell, J.M., M.W. Griffiths, S.A. McEwen, W.B. McNab and A.E. Yee, 1998. Antimicrobial drug residues in milk and meat: Causes, concerns, prevalence, regulations, tests and test performance: A review. J. Food Prot., 61: 742-756.

Mulchandani, A., W. Chen, P. Mulchandani, J. Wang and K.P. Rogers, 2001. Biosensors for direct determination of organophosphate pesticides. Biosens. Bioelectron., 16: 225-230.

Paige, J.C., L. Tollefson and M. Miller, 1997. Public health and drug residues in animal tissues. Vet. Hum. Toxicol., 30: 162-169.

Pecorelli, I., R. Bibi, I. Fioroni and R. Galarini, 2004. Validation of a confirmatory method for the determination of sulfonamides in muscle according to the European Union regulation 20002/657/EC. J. Chromatogr. A, 1032: 23-29.

Setford, S.J., E.R.M. Van, Y.J. Blankwater and S. Kroger, 1999. Receptor binding protein amperometric affinity sensor for rapid β-lactam quantification in milk. Anal. Chim. Acta, 398: 13-22.

Shull, L.R. and P.R. Chuke, 1983. Effect of synthetic and natural toxicants as livestock. J. Anim. Sci., 57: 330-354.

Sims, W.M. Jr., D.C. Kelley and P.E. Sandford, 1970. A study of aflatoxicosis in laying hens. Poult. Sci., 49: 1082-1084.

Smith, K.E., J.M. Besser, C.W. Hedberg, F.T. Leano and J.B. Bender *et al*., 1999. Quinolone-resistant *Campylobacter jejuni* infections in Minnesota, 1992-1998. N. Engl. J. Med., 340: 1525-1532.

Tanase, S., H. Tsuchiya, J. Yao, S. Ohmoto, N. Takagi and S. Yoshida, 1998. Reverse-phase ion-pair chromatographic analysis of tetracycline antibiotics: Application to discoloured teeth. J. Chromatogr. B Biomed. Sci. Appl., 706: 279-285.

Van Wendel de Joode, B., C. Wesselling, H. Kromhout, P. Moge, M. Garcia and D. Mergler, 2001. Chronic nervous system effects of long-term occupational exposure to DDT. Lancet, 357: 1014-1016.

Van Zytveld, W.A, D.C. Kelley and S.M. Dennis, 1970. Aflatoxicosis: The presence of aflatoxins or their metabolites in livers and skeletal muscle of chickens. Poult. Sci., 49: 1350-1356.