Food Science of Animal Resources

Food Sci. Anim. Resour. 2019 October 39(5):687~703
DOI https://doi.org/10.5851/kosfa.2019.e65

pISSN : 2636-0772 eISSN : 2636-0780
http://www.kosfaj.org

REVIEW

Reducing Veterinary Drug Residues in Animal Products: A Review

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OPEN ACCESS

Received	**July 5, 2019**
Revised	**August 20, 2019**
Accepted	**September 16, 2019**

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Abstract A survey we conducted suggests that the ingestion of veterinary drug residues in edible animal parts constitutes a potential health hazard for its consumers, including, specifically, the possibility of developing multidrug resistance, carcinogenicity, and disruption of intestinal normal microflora. The survey results indicated that antibiotics, parasitic drugs, anticoccidial, or nonsteroidal anti-inflammatory drugs (NSAIDs) are broadly used, and this use in livestock is associated with the appearance of residues in various animal products such as milk, meat, and eggs. We observed that different cooking procedures, heating temperatures, storage times, fermentation, and pH have the potential to decrease drug residues in animal products. Several studies have reported the use of thermal treatments and sterilization to decrease the quantity of antibiotics such as tetracycline, oxytetracycline, macrolides, and sulfonamides, in animal products. Fermentation treatments also decreased levels of penicillin and pesticides such as dimethoate, malathion, Dichlorodiphenyldichloroethylene, and lindane. pH, known to influence decreases in cloxacillin and oxacillin levels, reportedly enhanced the dissolution of antimicrobial drug residues. Pressure cooking also reduced aldrin, dieldrin, and endosulfan in animal products. Therefore, this review provides updated information on the control of drug residues in animal products, which is of significance to veterinarians, livestock producers, and consumer health.

Keywords veterinary drugs, residue, effect, withdrawal period, reduction

Introduction

Human beings consume protein-rich foods, mainly of animal origin (milk, meat, and eggs), to fulfill their nutritional requirements, and their health has been associated with the nature and quality of the food consumed (Rokka et al., 2005). Nevertheless, the quality of animal-based products is of great concern with regard to consumer health globally. Veterinary drugs such as antibiotics are generally used to enhance production, improve the feed conversion ratio, and treat diseases in food-producing animals (Beyene, 2016). However, the benefits of drug administration to farm animals used for food production are also accompanied by the risks associated with drug residues in the edible parts of treated animals (Boeckman and Carlson, 1995). Antimicrobial drugs, growth promoters, sedative drugs, anticoccidials, nonsteroidal anti-inflammatory drugs (NSAIDS), and anti-helminthics are the main veterinary drugs that potentially contaminate food-stuff (Beyene, 2016). Therefore, veterinary drug residues have been considered as a global food contamination challenge. Residues are defined as chemical substances or metabolites of medicinal products that may accumulate within the tissues or edible parts of treated animals (EC-European Commission, 2012). These residues may result from inappropriate or extra-label drug usage, failure to maintain drug withdrawal periods, or poor livestock production practices (Tajick and Shohreh, 2006). The treated animals may rapidly and efficiently metabolize some drugs while slowly and poorly metabolizing others; thus, the residues accumulate in the edible portion of the animals. Subsequently, consumers are exposed to these residues, resulting in health hazards (Babapour et al., 2012). Different cooking procedures, temperatures, and storage times, as well as the fermentation processes, have the potential to reduce veterinary drug residues (Heshmati, 2015). Hence, this paper aimed to review the potential sources of veterinary drug residues and their effects on the health of the public and highlight prevention, control, and reduction measures of drug residues in food producing animals.

Veterinary Drug Residues and Their Sources in Animal Products

Residues and chemical food contaminants arise from a variety of sources, including ingredients from natural toxins, industrial contaminants, agrochemicals/veterinary drugs, food processing, and packaging. Residues may also accumulate in animal tissues, depending on the drug's physicochemical properties and pharmacokinetic parameters. The major causes of drug residue accumulation in food-producing animals include improper observation of withdrawal periods, failure to maintain treatment records, overdose, or using prohibited drugs for economic animal treatment (Beyene, 2016). Contaminated animal feedstuffs also act as an important source of drug residues (Peeters et al., 2016) (Table 1).

Antibiotics

Antibiotics are very important, hence, widely used as veterinary medicine for therapeutic purposes as well as for prophylaxis and growth promotion. These substances inhibit DNA topoisomerases, protein synthesis, cell division and development, and/or cell wall synthesis of disease-causing or infectious microorganisms (Kohanski et al., 2010). Presently, approximately 80% of food animals receive antibiotics for part or most of their lifetime (Kibruyesfa and Naol, 2017), which may lead to residue accumulation in animal products. The presence of unexpected residues in foodstuff like meat, milk, and eggs may be attributable to unintentional or cross-contaminated feed in the pasture or feed mills, recirculation through manure and bedding materials, and antimicrobial-contaminated feed ingredients or water provided to the animal (Alebachew et al., 2016). However, antibiotic residue violation incidence has been observed globally. In Madagascar, the highest incidence rate of antibiotic drug residues was 37.2% in pork (Rakotoharinome et al., 2014). The residue violation rates of quinolone and penicillin increased in Korea, and the overall antimicrobial residue violation rate for different animal species was 0.5% (Kim et al., 2013). According to the Vietnamese antibiotic residues monitoring program, an average residue violation rate of 11.9% occurred in chicken, pork, and beef (Yamaguchi et al., 2015). In Malaysia, drug residues in chicken, swine, and cattle were monitored and the average violation rate was observed to be 2.7% (Marni et al., 2017). Meanwhile, Japan revealed that approximately 0.8% of antimicrobial drug residues were violated in 2012 (Yamaguchi et al., 2015) (Table 2).

Table 1. Stability of veterinary drug residues of animal origin

Veterinary drugs		Residue stability	References
Antibacterial	Aminoglycosides	- Neomycin and streptomycin are stable in milk with approximately 40% reduced by boiling.	Laszlo et al., 2018
		- Gentamicin residues are stable in chicken muscle.	Li et al., 2017
	Amphenicols	- Florfenicol is heat-labile in eggs and degraded (approximately 78%) via frying and boiling.	Filazi et al., 2015
		- Thermal treatment of meat degraded thiamphenicol by approximately 66%–82% in meat.	Franje et al., 2010
	Lactams	- Cloxacillin is the most heat-stable in milk and degraded by <10% after boiling. - Ampicillin was degraded by roughly 25% in milk during boiling and penicillin-G reduced by >40%. - Cephalexin reduced by approximately 40% in milk post thermal treatment.	Laszlo et al., 2018
	Quinolones	- Quinolone residues in milk were degraded by <10% when stored at 20°C. - Quinolones are very stable during thermal procedures and decreased by only 10% in milk.	Rozanska and Osek, 2013
		- Ciprofloxacin and norfloxacin were decreased by 12.71% and 12.01%, respectively, during thermal treatment of milk.	Roca et al., 2010
	Sulfonamides	- Sulfadiazine showed approximately 10% loss during milk boiling. - Sulfonamide residues are stable in animal tissues when frozen.	Laszlo et al., 2018
	Tetracyclines	- Pasteurization of milk decreased oxytetracycline and tetracycline residues by 40% and 30%, respectively.	Kellnerova et al., 2015
	Macrolides	- Lincomycin and tylosin are more heat stable in milk.	Heshmati, 2015
Adrenergic agonists	Clenbuterol	- Clenbuterol has a tendency not to degrade during storage.	Pinheiro et al., 2009
		- Different cooking procedures have no net effect on clenbuterol residues in incurred tissues.	Parr et al., 2016
Sedatives	Azaperone and azaperol	- Azaperone and azaperol residues are stable in pig kidney and liver under frozen conditions.	Aoki et al., 2009
Antihelminthics	Albendazole	- During milk storage, albendazole's concentration was barely affected.	Desmarchelier et al., 2018
	Levamisole	- Levamisole residues were decreased by 11% in fried muscle.	Cooper et al., 2011
	Rafoxanide	- Decreased by only 17%–18% in cooked muscle.	
	Carbadox	- Carbadox was stable in muscle.	Zhang et al., 2018

Antihelminthics

Owing to parasitic infections-induced economic losses, antihelmintic drugs are frequently used in livestock and, thus, have been associated with the appearance of residues in edible animal products. Illustratively, ivermectin is extensively used for the prevention and treatment of parasites in food-producing animals. Ivermectin is lipophilic, implying a long withdrawal period and presence in the edible parts of the treated animals, specifically those with high fat content (Baynes et al., 2000). In Ireland, bovine samples were screened and found positive for benzimidazole and avermectin (including ivermectin) residues (Teagasc, 2011). Furthermore, following dairy cattle antihelmintic treatment against gastrointestinal nematodes, antihelmintic drug residues were observed in cattle in Ireland, UK, Sweden, Belgium, and Germany (Bennema et al., 2010). However, residue exposure was higher in countries with a wider use of antihelmintic drugs and more locally consumed cattle products (Table 3). Interestingly, animals also absorb pesticides through a variety of routes; ingestion, inhalation, and dermal absorption.

Table 2. Violation status of antibiotic residues in animal products

Antibiotic	Animal food source	Residue level (μg/kg)	References
Tetracycline	Milk	16–134.5	Gaurav et al., 2014
	Cattle tissue	176.3	Abbasi et al., 2012
	Kidney	672.40	
	Liver	651.30	
Doxycycline	Poultry muscle	847.7	Jank et al., 2017
Sulfonamides	Milk	2.5	Kang et al., 2016
Gentamicin		90	Zeina et al., 2013
Streptomycin		80	
Penicillin		0–28	Abebew et al., 2014
Flumequine		2.58	Han et al., 2015
Enrofloxacin	Poultry (liver)	10–10,690	Sultan et al., 2014
	Cattle (liver)	30–3,610	
	Sheep (liver)	20–1,320	
Sulfonamides	Milk	13.5–147.9	Elizabeta et al., 2011
Sulfapyridine		1.77	Han et al., 2015
Sulfamethoxazole		4.2	
Lincomycin		11.25	
Quinolone	Chicken	30.81	Kim et al., 2013
	Beef	6.64	

Table 3. Violation status of antihelmintic residues in animal products

Antihelmintic	Animal food source	Residue level (μg/kg)	References
Ivermectin	Cattle (liver)	48	Escribano et al., 2012
	Sheep (liver)	43.7	
	Pig (liver)	23	
	Rabbit (liver)	15.8	
	Milk	2	
	Pigeon liver	58.5	Mestorino et al., 2017
Levamisole	Egg	599	Hossain et al., 2017
Oxyclozanide	Milk	130	Whelan et al., 2010
Levamisole		108	
Oxyclozanide	Soft cheese	5.6	
Levamisole		52	
Rafoxanide	Beef	28.6	Cooper et al., 2012
Doramectin		13.8	
Closantel	Milk (incurred)	41	Whelan et al., 2010
Benzimidazole	Bovine tissue	252.464	da Silva et al., 2017
Avermectin		100.025	
Moxidectin	Lamb (incurred)	20.95	Michelle Del Bianchi et al., 2018
Mebendazole	Pork	16.4	Lee et al., 2017

For instance, biotransformation of organochlorine pesticides into milk (via transfer of the absorbed active ingredient through the blood-milk barrier in the mammary gland) or measures for the prevention of pest infestation (spraying pesticide solutions on animals and their accommodation) contribute to bioaccumulation of persistent pesticides in animal-derived food (LeDoux, 2011) (Table 4).

Anticoccidials

Coccidiostats are compounds extensively used as additives or drugs for the prevention and treatment of livestock coccidiosis (Peek and Landman, 2011; Pura, 2013). Specifically, these drugs are used to treat or control the disease caused by organisms of the genus *Eimeria*, known to damage the intestinal mucosa of the host animal (Zhao et al., 2018). However, coccidiostats are also potent, causing residue accumulation in edible animal products and, consequently, posing serious health risks to the consumer (Kadykalo et al., 2018). Animals have been shown to rapidly metabolize anticoccidials, leading to harmful consequences; for example, metabolism of dimetridazole causes the release of the main metabolite, 2-hydroxydimetridazole, which accumulates highly in tissues and eggs (Mortier et al., 2005). The incidence of anticoccidial residues in edible animal products is very common. For instance, in Northern Ireland, the detectable concentrations of lasalocid ranged from 1.5–19 μg/kg (Matus et al., 2016). In the UK, eggs were monitored for the presence of different anticoccidials and proved positive for the corresponding residues such as robenidine (16 μg/kg), monensin (10 μg/kg), salinomycin (8 μg/kg), and lasalocid (129 μg/kg) (Mortier et al., 2005) (Table 5).

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

In veterinary practice, NSAIDs are widely used (singly or in combination with antibiotics) for treating inflammation, pain,

Table 4. Violation status of pesticide residues in animal products

Pesticide	Animal food source	Residue level (μg/kg)	References
Malathion	Milk	48	Kara et al., 2016
Lindane		80	Richhariya et al., 2017
2,2-Bis(4-chlorophenyl)-1,1-dichloroethylene dichlorodiphenyldichloroethylene		0.51	Fischer et al., 2011
Dieldrin		0.2	
Fluvalinate		1.82	
Endosulfan sulfate		0.22	
Diphenylamine		0.19	
Bifenthrin		0.1	
Cyfluthrin		1	
Diazinon		0.005–0.586	Salas et al., 2003
Chlorpyrifos		0.059	
Malathion		0.110	
Dichlorodiphenyldichloroethylene	Egg	2.5–4.4	LeDoux M, 2011
	Milk	1.3	
Simazine	Egg	30.1–59.5	
Atrazine		52.2	
Dichlorodiphenyldichloroethylene	Pork	1.2–3.4	

Table 5. Violation status of anticoccidial residues in animal products

Anticoccidial	Animal food source	Residue level (µg/kg)	Reference
Salinomycin	Beef	7.35	Zhao et al., 2018
Toltrazuril	Milk	27	Clarke et al., 2013
Dinitrocarbanilide	Chicken breast	13	Bacila et al., 2017
Lasalocid	Chicken	1.5–19	Matus et al., 2016
Monensin		1.7–27	
Ractopamine		2.1–32	
Lasalocid	Egg	129	Mortier et al., 2005
Nicarbazin		342	
Narasin		11	
Robenidine		16	
Monensin		10	
Salinomycin		8	
Dinitrocarbanilide		10	
Diclazuril	Chicken (liver)	161–469	Kang et al., 2015
Toltrazuril		104–525	
Amprolium		195–196	

respiratory diseases, fever, and musculoskeletal disorders (Gallo et al., 2010). They are equally used for improving animal production, and their secondary pharmacological effects enhance meat quality. However, after administration, these drugs bind to plasma proteins, are absorbed and distributed through tissues and fluids, and excreted as glucuronic conjugates (Rocca et al., 2017). NSAIDs are also frequently used for treating mastitis in pigs and milking cows, and the residues are excreted through milk (Jedziniak et al., 2012). Therefore, only few NSAIDs are approved for use in dairy cows. In the EU, MRLs have been established in milk; flunixin (40 µg/kg), meloxicam (15 µg/kg), tolfenamic acid (50 µg/kg), metamizole (50 µg/kg), and diclofenac (0.1 µg/kg). Nevertheless, some of these residues such as meloxicam (15.2 µg/kg), tolfenamic acid (54 µg/kg), and diclofenac (0.13 µg/kg) have been shown to exceed the maximum limit (Jedziniak et al., 2012). To maintain these residues within acceptable limits, they must be withheld with MRLs and legislation compliance adequately monitored (Table 6).

Decreasing Drug Residues in Animal Food Products

Proper drug use and good veterinary practices may lead to healthy and fresh edible animal products. However, the negative consequences of drug use, such as drug residues, continue to affect food; the levels of these residues sometimes exceed the limits of safe consumer levels. However, several drug-related factors such as drug formulation type, site, and route of administration, dose, and animal-related factors such as breed, age, sex, and body condition, have potential effects on the pharmacokinetics and drug residue levels in milk, meat, eggs, and other edible tissues (Moreno and Lanusse, 2017). Drug residue concentration in tissues depends on the physicochemical properties of the drug, such as acidic or basic properties and lipid solubility, which regulate the passive diffusion of drugs through cell membranes. Highly lipid-soluble drugs readily enter the intra and extracellular tissue compartments through passive diffusion, whereas drugs with poor lipid solubility

Table 6. Violation status of NSAID residues in animal products

NSAIDs	Animal food source	Residue level (μg/kg)	Reference
Acetyl salicylic acid	Pig	12–576	Kang et al., 2015
	Chicken	50–53	
Paracetamol	Pig	28–381	
Phenylbutazone	Chicken	247	
Oxyphenbutazone		15	
Flunixin	Milk	77	Feely et al., 2002
Meloxicam		15.2	Jedziniak et al., 2012
Tolfenamic acid		54	
Diclofenac		0.13	
Carprofen		4	Gallo et al., 2010
Flurbiprofen		2	
Vedaprofen		4	
Niflumic acid		20	
Mefenamic acid		10	
Naproxen		2	
Phenylbutazone	Bovine muscle	153.9	Asea et al., 2004

NSAIDs, nonsteroidal anti-inflammatory drugs.

remain in the extracellular compartment (Lees and Toutain, 2012). Drug transport modulation (such as several pharmacological approaches) delays bile or intestinal secretions, prolonging the macrocyclic lactone recycling time in the host, leading to transport protein (P-gp) efflux, which may be related to pharmacokinetic disposition and drug residue profiles (Lespine et al., 2012; Lifschitz et al., 2012). When this occurs, P-gp modulating agents change tissue residue patterns (Lespine et al., 2008). Interestingly, drug administration through animal ears helps prevent drug residue accumulation in edible animal tissues (Brown, 2000). However, most animal products are not consumed raw; hence, different heat treatments (pasteurization, sterilization, steaming, boiling, frying, or roasting) can cause drug residue loss through evaporation, co-distillation, and/or thermal degradation (Dordevic and Durovic-Pejcev, 2016). Furthermore, fermentation, different pH levels, and storage times also have a considerable impact on the reduction of drug residues in different edible products (Table 7).

Reduction of Drug Residues in Milk and Milk Products

Veterinary drug residues in milk remain a paramount concern to farmers, processors, milk regulatory agencies, and consumers because milk is widely consumed by people of all ages (Shaker and Elsharkawy, 2015). Veterinary drugs are broadly used to treat several cattle diseases or increase milk production. Consequently, drug residues are accumulated and secreted alongside milk (Han et al., 2015). However, before consumption, a majority of animal products undergo thermal treatment that leads to water loss, fat degradation, and protein denaturation, as well as an altered pH, which helps change drug residue quantity and chemical structure and, hence, the pharmacological and toxicological effects (Hsieh et al., 2011). For instance, heating milk via pasteurization, ultra-heat treatment (UHT), or sterilization, helps decrease drug residues in milk. The UHT, was shown to decrease oxytetracycline and tetracycline concentrations by >40% and 30%, respectively, and the

Table 7. Thermal reduction of antibiotic residues in animal food products as reported in literature

Antibiotic	Compound	Processing method	Matrix	Reduction (%)	References
β-Lactam	Oxacillin/dicloxacillin/cloxacillin	Boiling	Milk	8–64	Grunwald and Petz, 2003
	Ampicillin	Grilling/roasting	Meat	2.3–100	O'Brien et al., 1981
	Cephalonium/cephapirin/cefoperazoe/ amoxycillin/ampicillin/penicillinG/ cloxacillin	Boiling	Milk	0.1–100	Roca et al., 2011
Tetracycline	Tetracycline/oxytetracycline/ doxycycline/chlortetracycline	Boiling/ roasting/ microwave	Meat	42–100	Abou-Raya et al., 2013
	Tetracycline	Frying/ boiling	Egg	58–69	Alaboudi et al., 2013
Macrolide	Erythromycin/spiramycin/tylosin	Boiling	Milk	0–93	Zorraquino et al., 2011
	Ivermectin	Boiling/ frying	Meat	45–50	Slanina et al., 1989
Aminoglycoside	Gentamicin/kanamycin/neomycin/ streptomycin	Boiling	Milk	17–9	Zorraquino et al., 2009
Amphenicol	Chloramphenicol/florfenicol/ thiamphenicol	Boiling/ microwave	Meat	100	Franje et al., 2010
Quinolones	Ciprofloxacin/norfloxacin/ flumequine/oxolinic acid/ enrofloxacin	Boiling	Milk	0.01–12.71	Roca et al., 2010
	Enrofloxacin	Frying/ boiling	Egg	47–52	Alaboudi et al., 2013
Sulfonamides	Sulfamethazine/sulfachloropyridazine/sulfadiazine/sulfadimethoxine/ sulfamerazine/sulfapyridine/ sulfathiazole/sulfaquinoxaline	Boiling	Milk	0–85.1	Roca et al., 2013
Lincosamide	Lincomycin	Boiling	Milk	0–5	Zorraquino et al., 2011

sterilization process degraded tetracycline in milk by approximately 98% (Kellnerova et al., 2015). Furthermore, thermal treatment degrades macrolides in milk by approximately 93% and is mostly responsible for erythromycin susceptibility (Zorraquino et al., 2011). A majority of aminoglycosides are very unstable in milk, when boiled at 120℃ for 20 min, leading to elimination of approximately 95% aminoglycoside residues (Zorraquino et al., 2009).

During yoghurt production by heat treatment, precipitated proteins promote reduction of penicillin residues, and lactic acid slightly helps degrade cloxacillin, oxacillin, dicloxacillin, and nafcillin (Grunwald and Petz, 2003). Furthermore, yogurt cultures and low pH affect the decrease in drug residue concentration by occlusion in the coagulated protein matrix, decomposition, adsorption, and covalent binding to the proteins. During lactic acid-induced milk coagulation (pH 4), penillic acid concentration was shown to increase to 60%–90% and the residues comprised intact penicillin and penillic acid. At lower pH values (pH 2), further degradation occurred and unidentified products were observed after totaling penicillin G and penillic acid. It was also reported that heat treatment (pasteurization and sterilization) and fermentation helped to decrease organophosphorus pesticide residues in yoghurt (Zhang et al., 2006). Pasteurization helped to degrade pesticide dimethoate by as much as 73.42%, and, by fermentation, dimethoate and malathion concentrations decreased by 86.50% and 97.17%, respectively (Abd-Rabo et al., 2016). Moreover, when two starter cultures were added during yoghurt preparation, dimethoate, fenthion, and trichlorfon concentrations readily decreased (Regueiro et al., 2015).

Summary

- Thermal treatments: reduced tetracycline and oxytetracycline by 30% and 40%, respectively. Sterilization helped to degrade tetracycline by approximately 98%, reduce macrolides by 93%, reduce aminoglycosides residues by >95%, and degrade sulfonamides within a range of 0%–99%.
- Fermentation: reduced penicillin by 35%–40% and pesticide-like dimethoate and malathion by 86.5% and 97.17%, respectively.
- Altered pH: lactic acid (pH 4) at room temperature reduced cloxacillin and oxacillin residues by 20%–25%.

Reduction of Drug Residues in Eggs

When drugs are administered to laying hens, their metabolites may accumulate as residues in egg components (yolk and albumen) (EC-European Commission, 2012). These drugs are absorbed in the intestine, carried through blood/plasma to the ovary, and deposited in the inner yolk to the magnum of the oviduct for accumulation in the albumen, uterus, and the oviduct; and finally, during plumping of the eggs, drug residues are accumulated in the eggs (Donoghue and Myers, 2000). Drugs that quickly disappear from the body of the laying hen are also excreted rapidly from the egg component a few days post-withdrawal or treatment termination. Moreover, the biological half-life (drug residues reducing time) of the used drug is essential for drug residue clearance from egg components (Goetting et al., 2011).

Raw eggs are usually not consumed, unless refrigerated and subjected to heat. Heat treatment promotes dehydration, protein denaturation, and pH changes that can help reduce residue quantity, chemical formulation, as well as alter residue solubility. Consequently, frying and boiling eggs reduced the concentration of enrofloxacin and tetracycline residues by 69% and 58%, and 52% and 47%, respectively (Fath El-Bab, 2012). Furthermore, the residues of antimicrobials such as ciprofloxacin, enrofloxacin, and chlortetracycline, were reduced after eggs were boiled at 100°C for 15 min, by approximately 87%, 93%, and 61%, respectively (Alaboudi et al., 2013). However, chlorinated pesticides can diffuse into laying hens via feed, leading to residue excretion in eggs (Hashemy-Tonkabony and Mossofian, 1979). Effects of hard boiling and scrambling decreased the residue of chlorpyriphos in egg yolks by 38% (Bajwa and Sandhu, 2014). Adoption of best management practices in the poultry farms, feed quality monitoring, and breeding in confined areas can help decrease pesticide residues in eggs (Hamid et al., 2017). However, pH may differ in the albumen and yolk of fresh eggs (albumen; 7.6–7.9, yolk; 6.0), resulting to fading drug capabilities (Kan and Petz, 2000). High pH increases the fading capabilities of drugs with a naturally low pH value. For instance, the pH value of chlortetracycline is 2.3–3.3; hence, it has a relatively high binding affinity to the alkaline albumen than the acidic egg yolk (Alaboudi et al., 2013).

Egg refrigeration and storage also contributes to reducing antimicrobial residues in eggs. For instance, enrofloxacin and ciprofloxacin in eggs showed instability as refrigeration time increased, resulting in a 44%–50% reduction after 4 weeks of storage. Eggs refrigerated at 10°C for 4 weeks led to a decrease in the concentration of sulfanilamide and chlortetracycline residues by 44%–49% and 20%–22%, respectively (Alaboudi et al., 2013).

Mycotoxins such as aflatoxins and zearalenone are carried over in eggs; prolonged exposure in laying hens may result in residue deposition in eggs. Incorporating the *Bacillus subtilis* biodegradation products in the diet may decrease aflatoxins residue levels, causing specific toxin biotransformation and aiding inhibition of toxin absorption via the gastrointestinal tract; hence, decreasing the toxin residues in eggs (Jia et al., 2016). However, heating milk and dairy products with this quantity of aflatoxins M1 (AFM1) is obscure, and some treatments such as pasteurization and sterilization have very little effects on their concentration in the processed animal product. Conversely, milk processing such as evaporation, concentration, or drying, largely affect AFM1 concentration (Flores-Flores et al., 2015).

Summary

- Thermal treatments: reduced enrofloxacin and tetracycline residues by 52% and 47% and ciprofloxacin, enrofloxacin, and sulfanilamide residues by 87%, 93%, and 89%–91%, respectively, and chlorpyriphos residue by 38%.
- Storage: sulfanilamide reduced by 44%–49%, chlortetracycline by 20%–22%, and enrofloxacin and ciprofloxacin by 44%–50%.
- pH treatments: pH enhances the dissolution of antibiotic residues in egg components.

Reduction of Drug Residues in Meat

Uncontrolled usage of veterinary drugs and poor biosafety measures for drug withdrawal may result in drug residues, as well as decrease meat quality (Mehtabuddin et al., 2012). A majority of meat and meat products may not be an obvious part of the human food chain but are frequently stored or processed. Before consuming raw edible animal products and byproducts, some heat treatment or cooking is required. These processes lead to protein denaturation, water and fat loss, and change in the pH, thus, help in altering residue concentration, chemical structure, or solubility.

Doxycycline residue concentrations have been shown to reduce after meat cooking, and residues were excreted from muscle tissues into cooking fluid (Javadi, 2011). The biological activity of oxytetracycline, ampicillin, and chloramphenicol in beef also decreased by 12% to 50% after roasting at 50℃–90℃ for 20 min. Moreover, beef cooking contributed to a substantial decrease (35% to 94%) in oxytetracycline's net concentration (Gratacos-Cubarsí et al., 2007). Different cooking methods with different pH levels have a potential reduction effect on oxytetracycline. For instance, the muscle concentration of oxytetracycline was significantly reduced after roasting and boiling by 53.6% and 69.6%, respectively, and roasting, microwaving, and boiling at pH 6.0 and 7.2, decreased oxytetracycline levels by 34.3%, 53.2%, and 67.7%, respectively (Vivienne et al., 2018). In chicken and pork, different thermal treatments have potent degradation effects on oxytetracycline and produce oxytetracycline degradation products. Residual concentrations of oxytetracycline degrade as the sum of the corresponding epimeric forms (OTCs=OTC+4epi-OTC and apo-OTCs=α-apo-OTC+β-apo-OTC). After tissue thermal treatment, the concentrations of apo-OTCs increased whereas the OTC residues decreased (Nguyen et al., 2015). Therefore, the four epimers and anhydro forms of tetracycline may degrade under different conditions. The pathways associated with degradation of different tetracycline isoforms are mainly pH dependent, with the degradation of 4eTCs and anhydro-TCs being favored in dilute acidic medium, whereas in strong acidic medium, anhydro-TCs get cleaved and lactonized to generate apo derivatives (Xuan et al., 2009). Chicken meat boiling and roasting for 12 min decreased sulfonamide residues by 45%–61% and 38%–40%, respectively (Furusawa and Hanabusa, 2002).

pressure cooking accelerate pesticide degradation (aldrin; 93.75%, dieldrin; 93.77%, and endosulfan; 78.70%) in beef (Singh, 2017). Chemical and biological degradation occur during fermentation, and help decrease pesticide levels significantly (Azizi, 2011). For instance, the pesticide residues of DDT and lindane were reduced by approximately 10% and 18%, respectively, 72 h post-fermentation in fermented sausage (Abou-Arab, 2002). However, thermal treatment also helped to reduce antihelmintic residues: nitroxynil, by 78% and 96% in fried and roasted muscle; levamisole, by 11% and 42% in fried muscle and liver; rafoxanide, by 17% and 18% in fried and roasted muscle; and triclabendazole, by 23% and 47% in fried liver and roasted muscle, respectively (Cooper et al., 2011).

Summary

- Thermal treatments: oxytetracycline, ampicillin, and chloramphenicol residues were decreased by 12%–50%, sulfonamide residues by 45%–61%, and antihelmintic residues by 11%–96%.
- Pressure cooking: aldrin, dieldrin, and endosulfan were reduced by 79%–94%.
- Fermentation treatments: DDT was reduced by 10% and lindane by 18%.

Conclusion

The use of veterinary drugs for disease prevention or treatment and/or production enhancement, leads to residue accumulation in animal products. Drug residues in animal products are influenced by many factors such as the physicochemical properties of drugs, biological processes of animals, and their products. These residues can cause significant public health hazards such as hypersensitivity reactions, cancer, mutagenicity, reproduction challenges, bacterial resistance, and disruption of intestinal normal flora. Therefore, it is the responsibility of veterinarians and livestock producers to observe the relevant drug withdrawal period before animal slaughter and ensure that undesirable residues do not accumulate in edible products. Veterinarians should be updated with the latest information, to create awareness among producers and employees, as well as the general public. Moreover, avoiding unapproved or illegal drugs and practicing proper drug use and best farm and livestock management can lead to the control of drug residues. Moreover, different cooking conditions (temperature and time), fermentation, and pH, play a major role in decreasing veterinary drug residues. Generally, cooking and other processes do not ensure full drug residue degradation, but can contribute to a marked decrease in concentration. Although some veterinary drug residues are reduced and degraded by processing, it is essential to perform toxicology experiments to monitor the potential adverse effects of drug residues on consumer health.

Conflict of Interest

The authors declare no potential conflict of interest.

Acknowledgments

This work was supported by Korea Institute of Planning and Evaluation for Technology in Food, Agriculture, Forestry and Fisheries (IPET) through Agri-Bio industry Technology Development Program, funded by Ministry of Agriculture, Food and Rural Affairs (MAFRA) (316029-03-2-HD050).

Author Contributions

Investigation: Rana MS. Writing original draft: Rana MS, Hur SJ. Writing review & editing: Rana MS, Lee SY, Kang HJ, Hur SJ.

Ethics Approval

This article does not require IRB/IACUC approval because there are no human and animal participants.

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