



# Impact of Cooking Procedures on Antibacterial Drug Residues in Foods: A Review

A. Heshmati\*

Department of Nutrition, Medicine Faculty, Hamadan University of Medical Sciences and Health Services, Hamadan, Iran

## Article type

Review article

## Abstract

## Keywords

Cooking  
Drug Residues  
Food Safety

Received: 11 Nov 2014

Revised: 21 Dec 2014

Accepted: 15 Jan 2015

Antibacterial drugs used in animal might result in deposition of residues in meat, milk and eggs. The presence of antimicrobial residues in animal-originated food is critical problem in many countries over the years. Because, drug residues might result in various health hazards, both actual incidence of reactions and potential hazards perceived by the public, the most countries assess residue occurrences in food to provide a safe food supply and forbid importation of unwholesome foods from exporting countries. Stability of antibacterial drug residues under cooking conditions is an important research field, which provides valuable information related to health safety aspects and is very important from a safety and toxicological point of view. It has been stated that drug residues in animal based foods may be decreased due to cooking. Stability of antibacterial residues during heating is different. In this article, the changes of antibacterial drug residues during different cooking procedures are reviewed. Ordinary cooking procedures degrade a number of antibacterial drug residues, depending on the amount of heat treatment involved. Cooking time and temperature are two main factors which affect on antibiotic residues. In some cooking procedures, sufficient heating temperature and time can reduce several antibacterial drug residues although it does not generally provide an additional margin of safety for consumers.

## Introduction

Antibacterial drugs are largely used in animals for three objectives including therapeutic application to treat disease in animals, prophylactic utilization to prevent infection in animals, and growth promoters to improve feed utilization and production (Barton, 2000; Heshmati et al., 2013). Antibacterial drugs used in animal might result in deposition of residues in meat, milk and eggs. The presence of antimicrobial residues in animal-originated food is critical problem in many countries over the years (Kaneene and Miller, 1997). Because, drug residues might result in various health hazards, both actual

incidence of reactions and potential hazards perceived by the public, the most countries assess residue occurrences in food to provide a safe food supply and forbid importation of unwholesome foods from exporting countries. Although goals of all countries are to assure a safe food resource for human, practices of veterinary drug utilization, acceptable residue level and procedures applied for measurement of residues in foods vary from one country to other country and change over time. Therefore, the objective of this paper would be to illustrate the changes of antibacterial drug residue during various cooking procedures (Heshmati et al., 2013; Heshmati et al., 2014).

\*Correspondence

E-mail: a.heshmati@umsha.ac.ir

### Health problems associated with antibiotic residues

Occurrence of antibacterial residues in animal-originated foodstuffs could pose consumers health risk. Antibiotic residues in food are potential threat to direct toxicity in human and their low levels would result in death of intestinal flora, cause disease and the possible development of resistant strains which cause failure of antibiotic therapy in clinical situations. However, the principal hazardous effect is likely to develop the resistance of bacteria following the ingestion of sub-therapeutic doses of antimicrobials. The resistance could be transferred from nonpathogenic microorganisms to pathogenic ones, which would then no longer respond to normal drug treatment (Heshmati et al., 2015).

The illicit use of antibiotics could thus increase the risk of food-borne infection with antibiotic-resistant pathogenic bacteria contaminating food taken by human. Other harmful effects related to antibiotic residues in food include immune pathological effects, autoimmunity, carcinogenicity (sulphamethazine, oxytetracycline, furazolidone), mutagenicity, nephropathy (gentamicin), hepatotoxicity, reproductive disorders, bone marrow toxicity (chloramphenicol), and allergy (penicillin) (Heshmati et al., 2013; Nisha, 2008).

Toxic effects are not probable because residue contents in food are in very low concentrations. Nevertheless, some substances must receive particular attention owing to their harmfulness. Allergic reactions may also be produced in sensitive or sensitized individuals.

For protecting human from exposure of any veterinary residues, a withdrawal time has been determined. The withdrawal time is defined as the time interval from administration of a drug to animal until slaughter to assure that drug residues in meat are below maximum residue limit (Heshmati et al., 2013; Heshmati et al., 2014).

Veterinary drug residue contents in animal-originated food depend on various factors such as drug dosage, type and age of animal, feeding, disease status, poor management, extra-label drug use, withdrawal time, and route of administration (Codex Alimentarius Commission, 2001; Kaneene and Miller, 1997). In addition, it has been shown different factors affect residues after slaughter. Although most investigations have been focused on prevention and detection of residues, some researches have been conducted on the changes of residues in tissues during storage and cooking. Before consumption, most animal-originated food is cooked or underwent various processing such as food additive treatments to increase digestibility, sensory properties, appetizing attribute and shelf-life. The Codex Alimentarius Commission of the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) of the United Nations have stated that the scientific literatures about influence of

processing on drug veterinary residues in food are inadequate to consider clear determination, therefore additional studies are needed in this area (Codex Alimentarius Commission, 2001) because veterinary drug residues vary in their susceptibility to degrade by heating. Some previous studies were based on the estimation of microbiological activity loss after heat treatment. By assessing the lost of microbiological activity, it is impossible to calculate precise content of residues that were reduced during thermal processing and degradation kinetics. In recent years, HPLC and LC-mass were applied to assess changes of veterinary drug residue during processing (Hassani et al., 2008; Heshmati et al., 2013; Heshmati et al., 2014). The recent review was conducted on the effects of cooking on antibacterial drugs residues in foods.

### Stability of tetracycline residues during cooking

Generally, tetracycline (TC) residues are considered relatively unstable compounds. Temperature during cooking has the largest impact on the loss of tetracycline residues (Abou-Raya et al., 2013; Du et al., 1997; Fedeniuk et al., 1997; Hassani et al., 2008; Honikel et al., 1978; Ibrahim, 1994; Kitts et al., 1992; Loksuan, 2002; Moats, 1999; O'Brien et al., 1981; Rose et al., 1996). It was shown that oxytetracycline residue in cattle liver and muscle and sheep muscle was reduced during cooking processes including microwaving, boiling, roasting, grilling, braising and frying about 35-94% (Rose et al., 1996).

Abou-Raya et al. (2013) studied the changes by microwave, boiling and roasting cooking processes on TCs including oxytetracycline (OTC), tetracycline (TTC), chlorotetracycline (CTC) and doxycycline (DOC) in chicken breast and thigh, and determined the cooking time required to make the cooked sample safer for consumption.

Cooking procedure was one of the most important agents that influenced TC residues. Among various procedures studied, microwaving was the most effective one. It is obvious that the more cooking time, the greater loss of residue. During heat processing, it was identified the most stable and the most unstable TCs are doxycycline and oxytetracycline, respectively. The time required to destroy 90% of the initial TCs contents are 23.9, 53.2 and 101.6 min for microwaving, boiling and roasting, respectively. If cooking temperature and time are sufficient, we could assure significant losses of TC residues. Therefore, it was said cooking provides safety margin for products containing TCs (Du et al., 1997; Fedeniuk et al., 1997; Hassani et al., 2008; Ibrahim, 1994; Kitts et al., 1992).

In study of thermo stability of oxytetracycline, tetracycline, and doxycycline at ultrahigh temperature, it was identified that their destruction follows a first-order reac-

tion kinetic. Regarding sterilization, whereas low temperature-long time treatments (conventional sterilization) would destroy >98% of the initial concentration of the residues of the three antibiotics, high-temperature-short-time treatments (HTST) would leave unaltered residues in the 50–90% range (Hassani et al., 2008).

#### Stability of $\beta$ -lactam residues during cooking

Food processing affects on penicillin residues. Many factors were effective on penicillin residue. Grunwald and Petz (2003) found that  $\beta$ -lactam residue in yogurt is influenced by heating treatment applied for the milk before adding starter cultures, the fermentation temperature and time, and the penicillin binding to milk proteins. During yogurt production, benzylpenicillin (penicillin G) and cloxacillin were degraded. Therefore, during yogurt production, penicillin residues are decreased (Grunwald and Petz, 2003).

Losses of benzylpenicillin during cooking are proportional to the harshness of heat regime and some fluids were released during the cooking process (Rose et al., 1997). By discarding any juices which come from the meat during cooking; it can reduce exposure to residues of benzylpenicillin.

Some microorganisms found in raw milk produce penicillinase that degrades penicillin during storage and processing. Since heating processes inactivate penicillinase, it has been suggested that benzylpenicillin is more stable in UHT treated milk than in raw milk (Rose et al., 1997).

#### Stability of macrolide residues during cooking

Little information was found on the effects of food processing on macrolide residues. The stability of some macrolide residues such as oleandomycin was highly dependent on the type of the food matrix in which it is contained (Botsoglou and Fletouris, 2001). In study done to investigate the effect of milk heating to diminish the antimicrobial activity of macrolides residue, it was identified heat treatment have different effects. Sterilization at 120 °C for 20 min inactivates 93% of erythromycin, 64% of spiramycin, 51% of tylosin and 5% of lincomycin. Treatment at 140 °C for 10 s resulted in erythromycin, spiramycin, tylosin and lincomycin reduction about 30%, 35%, 12% and 5%, respectively. Pasteurization (60 °C for 30 min) reduced 21% and 13% of antimicrobial activity from erythromycin and spiramycin, respectively (Zorraquino et al., 2011).

It was found that tylosin and tylosin residue reduced during chicken cooking. Reduction percentage is in significant and positive correlation with cooking time, sample weight percent and center temperature. Because the whole cooked product is consumed, measuring

tylosin concentration in raw tissue could not be applied for consumer exposure and dietary intake calculations when the whole cooked product is consumed. It is verified that cooking reduced macrolide residues in meat although, it is necessary to regard correct consumption of veterinary drug in animals and withdrawal time (Heshmati et al., 2013; Heshmati et al., 2014; Heshmati et al., 2015).

#### Stability of nitrofurans residues during cooking

In animal, nitrofurans are rapidly metabolized to 3-amino-2-oxazolidinone (AOZ), 3-amino-5-morpholinomethyl-2-oxazolidone (AMZO), 1-aminohydantoin (AHD) and semicarbazide (SEM). These metabolites are tissue-bound and stable which may be released by mild acid hydrolysis and therefore used as marker residues (Cooper and Kennedy, 2007). Furazolidone residues are decreased at postmortem because active enzymes remained for long periods after animal death convert furazolidone to its metabolite (Steffenak et al., 1991). Cooper and Kennedy (2007) found that frying, grilling, roasting and microwaving did not affect nitrofurans metabolites in muscle and liver of pigs. Therefore, they concluded these metabolites are largely stable to traditional cooking procedures and present human health risk.

#### Stability of quinolone residues during cooking

Cooking is not effective in residues amounts of the quinolones such as oxolinic acid and flumequine in fish. Both compounds were not degraded during fish cooking. Its reported enrofloxacin and ciprofloxacin residues in flatfish had high heating stability (Botsoglou and Fletouris, 2001). The influence of different cooking procedures (microwaving, roasting, boiling, grilling and frying) on naturally incurred enrofloxacin residues in chicken muscle was studied. Lolo et al. (2006) concluded cooking procedures did not reduce enrofloxacin residues; therefore, this residue retained its stability during heating. During boiling treatment, some quinolones were extracted into broth. In cooking procedure with water loss, quinolone residues were increased (Lolo et al., 2006).

Roca et al. (2010) found quinolones are very stable during thermal procedures. At 120 °C for 20 min, the maximum losses of concentration ciprofloxacin and norfloxacin were 12.71% and 12.01%, respectively (Roca et al., 2010). Therefore, because quinolone residues were not degraded during processing, their present in food threaten human health (Roca et al., 2010).

#### Stability of amphenicol residues during cooking

Several investigations on the stability of chloramphenicol during thermal treatment have been also carried out.

Epstein et al. (1988) found that chloramphenicol was partially degraded by curing and cooking. More severe heating such as pretreatments of canning resulted in total degradation. In addition to cooking process, the stability of chloramphenicol is also markedly affected by emulsifying and curing (Epstein et al., 1988). Furthermore, the stability of CAP during different storage temperatures was studied. The chloramphenicol stability in muscle during refrigeration and freezing storage conditions was high although milk freezing decreased its content significantly (Ramos et al., 2003). Shakila et al. (2006) reported heat stability of chloramphenicol residue is low and this component is destroyed or degraded during cooking procedure and its loss was dependent on time and temperature increment.

### Stability of sulfonamide residues during cooking

In past, it was said sulfonamides are heat stable compounds. In recent research, it was identified residues of sulfadiazine (SDZ), sulfamethoxazole (SMX), sulfamonomethoxine (SMM) and sulfaquinoxaline (SQX) in chicken meatball was reduced during boiling (45-61%), roasting (38-40%) and microwaving (35-41%). The reduction observed for the present cooking methods may be explained by (1) transfer of veterinary drug residue from the muscle into the boiling water; and (2) loss of juices which came from the muscle as it was roasted (Furusawa and Hanabusa, 2002). Different times (3, 6, and 9 min) and temperatures (170, 180 and 190 °C) of deep-frying had different effects on SDZ, SMZ, SMX, and SQX residues in chicken meatball. Generally, frying time was more effective than frying temperature. The increase of internal temperature during deep-frying procedure and the weight loss of the chicken meatballs after frying were two factors influenced in sulfonamide reduction. Generally, by increasing of deep-frying time and temperature, the lower sulfonamide concentrations were found in meatball. The maximum reductions observed in chicken meatball for SDZ, SMZ, SMX, and SQX were 37.5, 27.5, 40.7, and 27.6%, respectively (Ismail-Fitry et al., 2008). It is known that fermentation step during sausage production affect on SMZ and sulfapyrazine residues and resulted in remaining of less than 40% of mentioned compounds after ripening for 10 days. During manufacture of raw fermented sausages, Smit et al. (1994) found 25% of the sulfadimidine was lost in the brine.

### Conclusion

In this review, effects of various cooking procedures on different antibacterial drug residues were explained. According to the results and findings of previous researches, we can conclude cooking time and temperature play ma-

nor role among the various agents affect antibiotic residues after cooking process. Generally, cooking processes do not assure a full break-down of different antibacterial drug residues present in food originated animals and they can only decrease their amounts. The most of residues during boiling procedure excreted from tissue to cooking fluid therefore it is advised to discard any meat broth in order to reduce exposure to residues. Some drug residues are stable to cooking and, therefore, data obtained from surveillance of raw samples for residues of those drugs can be assumed to be directly applicable in calculating dietary exposure and consumer intake. Although some drug residues were decreased and degraded during cooking, it is necessary to performed toxicology experiments for effects of their metabolites on human body.

### Conflicts of interest

None declared.

### References

- Abou-Raya S., Shalaby A.R., Salama1 N.A., Emam W.H., Mehaya F.M. (2013). Effect of ordinary cooking procedures on tetracycline residues in chicken meat. *Journal of Food and Drug Analysis*. 21: 80-86.
- Barton M.D. (2000). Antibiotic use in animal feed and its impact on human health. *Nutrition Research Reviews*. 13: 279-299.
- Botsoglou N.A., Fletouris D.J. (2001). Stability of residues during food processing. Marcel Dekker, Inc, New York.
- Codex Alimentarius Commission. (2001). Committee on residues of veterinary drugs in foods, document control of veterinary drug residues in milk and milk products. Joint food and agriculture organization of the united nations–world health organization food standards programme, Rome.
- Cooper K.M., Kennedy D.G. (2007). Stability studies of the metabolites of nitrofurantoin antibiotics during storage and cooking. *Food Additives and Contaminants*. 24: 935-942.
- Du W.X., Marshall M.R., Xu D.H., Santerre C.R., Wei C.I. (1997). Retention of oxytetracycline residues in cooked channel catfish filets. *Journal of Food Science*. 62: 119-122.
- Epstein R.L., Randecker V., Corrao P., Keeton J.T., Cross H.R. (1988). Influence of heat and cure preservatives on residues of sulfamethazine, chloramphenicol, and cyromazine in muscle tissue. *Journal of Agricultural and Food Chemistry*. 36: 1009-1012.
- Fedeniuk R.W., Shand P.J., Mccurdy A.R. (1997). Effect of thermal processing and additives on the kinetics of oxytetracycline degradation in pork muscle. *Journal of Agricultural and Food Chemistry*. 45: 2252-2257.
- Furusawa N., Hanabusa R. (2002). Cooking effects on sulfonamide residues in chicken thigh muscle. *Food Research International*. 35: 37-42.
- Grunwald L., Petz M. (2003). Food processing effects on residues: penicillins in milk and yoghurt. *Analytica Chimica Acta*. 483: 73-79.
- Hassani M., Lázaro R., Pérez C., Condón S., Pagán R. (2008). Thermostability of oxytetracycline, tetracycline, and doxycycline at ultrahigh temperatures. *Journal of Agricultural and Food Chemistry*. 56: 2676-2680.
- Heshmati A., Kamkar A., Salaramoli J., Hassan J., Jahed G.H. (2013). The effect of two methods cooking of boiling and microwave on tylosin residue in chicken meat.

- Iranian Journal of Nutrition Sciences and Food Technology*. 8: 61-71.
- Heshmati A., Kamkar A., Salaramoli J., Hassan J., Jahed G.H. (2015). Effect of deep-frying processing on tylosin residue in meat. *Iranian Journal of Nutrition Sciences and Food Technology*. 12: 61-71.
- Heshmati A., Salaramoli J., Kamkar A., Hassan J., Jahed G.H. (2014). Experimental study of the effects of cooking methods on tilmicosin residues in chicken. *Journal of Veterinary Research*. 69: 283-290.
- Honikel K.O., Schmidt U., Woltersdorf W., Leistner L. (1978). Effect of storage and processing on tetracycline residues in meat and bones. *Journal of Association of Official Analytical Chemists*. 61: 1222-1227.
- Ibrahim A. (1994). Effect of cooking procedures on oxytetracycline residues in lamb muscle. *Journal of Agricultural and Food Chemistry*. 42: 2561-2563.
- Ismail-Fitry M.R., Jinap S., Jamilah B., Saleha A.A. (2008). Effect of deep-frying at different temperature and time on sulfonamide residues in chicken meat-balls. *Journal of Food and Drug Analysis*. 16: 81-86.
- Kaneene J.B., Miller R. (1997). Problems associated with drug residues in beef from feeds and therapy. *Review of Scientific Technology Office of International Epizootics*. 16: 694-708.
- Kitts D.D., Yu C.W.Y., Aoyama R.G., Burt H.M., Mcerlane K.M. (1992). Oxytetracycline degradation in thermally processed farmed salmon. *Journal of Agricultural and Food Chemistry*. 40: 1977-1981.
- Loksuwan J. (2002). The effect of heating on multiple residues of tetracyclines in milk. *Thammasat Internatinal Journal of Science Technology*. 7: 17-21.
- Lolo M., Pedreira S., Miranda J.M., Vazquez B.I., Franco C.M., Cepeda, A., Fente C. (2006). Effect of cooking on enrofloxacin residues in chicken tissue. *Food Additives and Contaminants*. 23: 988-993.
- Moats W.A. (1999). The effect of processing on veterinary residues in foods. *Advances in Experimental Medicine and Biology*. 459: 233-241.
- Nisha A.R. (2008). Antibiotic residues-a global health hazard. *Veterinary World*. 1: 375-377.
- O'Brien J.J., Campbell N., Conaghan T. (1981). Effect of cooking and cold storage on biologically active antibiotic residues in meat. *Journal of Hygiene*. 87: 511-23.
- Ramos M., Aranda A., De Pozuelo M.M., Reuvers T. (2003). Chloramphenicol residues in food samples: their analysis and stability during storage. *Journal of Liquid Chromatography and Related Technologies*. 26: 2535-2549.
- Roca M., Castillo M., Marti P., Althaus R.L., Molina M.P. (2010). Effect of heating on the stability of quinolones in milk. *Journal of Agricultural and Food Chemistry*. 58: 5427-5431.
- Rose M.D., Bygrave J., Farrington W.H.H., Shearer G. (1996). The effect of cooking on veterinary drug residues in food: 4. Oxytetracycline. *Food Additives and Contaminants*. 13: 275-286.
- Rose M.D., Bygrave J., Farrington, W.H., Shearer G. (1997). The effect of cooking on veterinary drug residues in food. Part 8. Benzylpenicillin. *Analyst*. 122: 1095-1099.
- Shakila R.J., Vyla S. A.P., Saravana K.R., Jeyasekaran G., Indra J.G. (2006). Stability of chloramphenicol residues in shrimp subjected to heat processing treatments. *Food Microbiology*. 23: 47-51.
- Smit L.A., Hoogenboom L.A.P., Berghmans M.C., Haagsma N. (1994). Stability of sulfadimidine during raw fermented sausage preparation. *Zeitschrift für Lebensmittel-Untersuchung und-Forschung*. 198: 480-485.
- Steffenak I., Hormazabal V., Yndestad M. (1991). Reservoir of quinolone residues in fish. *Food Additives and Contaminants*. 8: 777-780.
- Zorraquino M.A., Althaus R.L., Roca M., Molina M.P. (2011). Heat treatment effects on the antimicrobial activity of macrolide and lincosamide antibiotics in milk. *Journal of Food Protection*. 74: 311-315.