OXFORD

Food Quality and Safety, 2019, 3, 233–241
doi:10.1093/fqsafe/fyz035
Review
Advance Access publication 5 November 2019

Review

Two perspectives of *Listeria monocytogenes* hazards in dairy products: the prevalence and the antibiotic resistance

Beyza H. Ulusoy and Kefyalew Chirkena

Faculty of Veterinary Medicine, Department of Food Hygiene and Technology, Near East University, Nicosia, Cyprus

Correspondence to: Beyza H. Ulusoy, Near East University, Near East Boulevard 99138, Nicosia/TRNC. E-mail: kolayisim@gmail.com

Received 1 August 2019; Revised 22 August 2019; Editorial decision 8 September 2019.

Abstract

Listeria monocytogenes is among the most food-borne pathogens. It has the ability to grow over a range of temperature, including refrigeration temperature. Foods kept in refrigerator more than the prescribed period of time create an opportunity for the occurrence of *Listeria monocytogenes.* As this review shows, the prevalence of *L. monocytogenes* has more likely evident in pasteurized milk than other dairy products, such as raw milk. Inadequate temperature and faults in technology during pasteurization can be the disposing factors for the presence of the organism in dairy products. The organism, on the other hand, has been found to be resistant to those commonly known antibiotics that have human and veterinary importance, namely, ampicillin, Tetracycline, and chloramphenicol, streptomycin, erytromycin, penicillin G., and others. Resistance ability of the organism can be mediated by different natural and acquired resistance mechanisms, such as self-transferrable plasmids, mobilizable plasmids, and conjugative transposons. The emergence and spread of antibiotic resistance of *L. monocytogenes* has serious public health and economic impacts at large. This paper has reviewed the prevalence and the antibiotic resistance of *L. monocytogenes* isolates of dairy products and the strategic mechanisms of the organism develop resistance against the antibiotics.

Key words: Listeria *monocytogenes*; prevalence; antibiotic resistance; dairy products.

Introduction

Food-borne diseases are mostly associated with microbial contamination due to improper food handling during production, processing, storage, and transportation (Martinović *et al.*, 2016). Mostly the diseases are evident in developing countries where poverty, illiteracy, poor hygienic conditions, and environmental sanitation and lack of infrastructure can be the disposing factors for the outbreaks of the diseases. On the other hand, modern lifestyle has significantly changed food-eating habits globally, particularly in developed countries, with a consequent increased need for ready-to-eat foods and take away foods which are frequently consumed (Lopez-Valladares *et al.*, 2018) and subsequently pose a potential risk to the consumers when they are contaminated by pathogens (Ndieyira *et al.*, 2017).

Listeriosis is one of the most serious and severe food-borne diseases and it is caused by *Listeria monocytogenes* (WHO, 2003). The organism contaminates food items at any production stages before consumption. Following consumption, the pathogen passes the intestinal barrier and spreads to the blood and lymphatic system to reach the liver and spleen, where it can multiply (Andersson *et al.*, 2015). *Listeria monoctogenes* is considered as an opportunistic human pathogen causing meningitis or septicaemia, especially infections among pregnant women, elderly, or individuals with weakened immune system. Immuno-compromised individuals are particularly vulnerable to this intracellular pathogen (Ramaswamy *et al.*, 2007). It can seriously infect the foetus in the pregnant women as it vertically transmits from mother to foetus through placenta (Cossart, 2011). The report of WHO (2018b) shows that pregnant women are about 20 times more likely to get infection by listeriosis than healthy adults as the disease can result in miscarriage or stillbirth and people with HIV/AIDS are at least 300 times more likely to get sick than those with normal immune system.

Some studies have revealed food products such as cheese, raw milk, and other dairy products as the main sources of *L. monocytogenes* and also consider as risk for food of humans (Lungu *et al.*, 2011; Seyoum *et al.*, 2015). Additionally, food products stored in vacuum or in modified atmospheres and extended refrigerator provide an opportunity for the bacterium to multiply to large numbers toward the end of the shelf life (Lopez-Valladares *et al.*, 2018). The source of *L. monocytogenes* in raw milk is mainly the gastrointestinal tract of animals and the environment. A study conducted on the prevalence of *L. monocytogenes* isolates of milk samples and other dairy products indicated that the organism can be found even in the balance tank of the pasteurizer and corresponding sample of pasteurized milk collected after pasteurization (72.6°C for 15 s) under high-temperature short-time (Navratilova *et al.*, 2004). Contamination of milk after pasteurization or due to defects in technology during pasteurization (inadequate temperature, technical errors) is responsible for the presence of *L. monocytogenes* in pasteurized milk. Therefore, the occurrence of *L. monocytogenes* in dairy milk because of failure in the pasteurization process or post-pasteurization contamination is still a concern (Lee *et al.*, 2019).

Listeria monocytogenes is the major concern for the food quality and safety in food industries, because it has the ability to form biofilms which can resist the standard cleaning and disinfection procedures (Centorame *et al.*, 2017). Antibiotics have been commercially available for long time for the treatment of infectious diseases, including those of food-borne infections. However, the resistance of microorganisms against these antibiotics has been also developing over this same period of time (Lungu *et al.*, 2011), and thus, it has become worldwide. The emergence and development of antibiotic-resistant microorganisms, which of mostly food-borne pathogenic bacteria, such as *Salmonella, Staphylococcus aureus, Escherichia coli, L. monocytogenes*, and other pathogens in food products, like dairy products, has been the challenge for food-processing industries as these microorganisms can easily able to contaminate food products, leading to reduce their shelf life during storage of foods in extended time (Leong *et al.*, 2014).The resistance of such pathogens to antibiotics may be arisen from misuse of antibiotics, for instance, in the treatment of diseases in animals and humans and as growth promoter for animals, and this in turn poses some serious health problems to the public (Rahimi *et al.*, 2012).

The emergence of *L. monocytogenes* in food products like dairy products and others is due to the antibiotic resistance of the organism. Olaimat *et al.* (2018) reviewed on the emergence of antibiotic resistance among *L. monocytogenes* strains isolated from food products and possible ways the resistance has developed. Due to this emergence of antibiotic resistance of the pathogen, future outbreaks and spread of the diseases may be hard to manage. Extensive monitoring and assessment on the prevalence and antibiotic resistance of this pathogenic microorganism in foods processed in different industries is more important to control and manage the dissemination of disease caused by *L. monocytogenes*. Therefore, the objective of this paper is to review on the prevalence and antibiotic resistance of *L. monocytogenes* isolates of dairy products.

Sources of Dairy Milk Contamination With *L. monocytogenes*

Silage, inadequate hygiene, sanitation, and housing conditions are the source of *L. monocytogenes* contamination in raw milk and the dairy environment. Besides to this, bulk tank milk, milk filter, milking machine, milk handler, faecal contamination, poor on-farm hygiene during milking, storage, and transportation are also considered as the source of contamination (Pantoja *et al.*, 2012). On the environment of dairy farm, once contamination occurs, it can easily be disseminated to the animals and from animals to animals (Hunt *et al.*, 2012). Food products are mostly contaminated by *L. monocytogenes* at any stage of production and processing lines. The organism can enter the food chain from 'farm to fork' through carrier animals that shed the organism directly to foods, which most likely increase the risk associated with contamination of raw milk and other food items (Hunt *et al.*, 2012). Most animals may be asymptomatic carriers shedding *L. monocytogenes* in dairy products for months (Bangieva and Rusev, 2017).

The most common route of infection to humans is through consumption of contaminated milk and milk products. It is a fact that one of the hygienic requirements for foods of animal origin is the absence of pathogenic microorganisms such as bacteria, protozoa, fungi, and viruses; however, at the time of the absence of hygienic conditions, foods become easily exposed to those pathogens to cause infection to humans after consumption. Therefore, human listeriosis is the disease associated with the consumption of foods of animals' origin such as dairy products contaminated by *L. monocytogenes*, particularly (Pitt *et al.*, 2000). Additionally, humans can acquire *L. monocytogenes* through foods kept in the refrigerators more than the prescribed time (greater than 5 days) (CFS, 2014), particularly ready-to-eat foods with long shelf-life under refrigerator.

The Prevalence of *L. monocytogenes* in Dairy Products

The occurrence of *L. monocytogenes* is worldwide and it is distributed widely in the environment. It has been considered as a potential contaminant of raw milk and other dairy products, including various types of foods. It is obvious that pasteurization of milk can kill *L. monocytogenes*, but it is appeared in the milk after pasteurization contamination and may be due to inadequate temperature and technical errors. Some literatures indicate that cleanliness of the animals' udder, milking equipment, milking man (handlers), health of the animals, and sanitation of dairy unit and shed can be the determinant factors in the microbial contamination of unpasteurized milk (Mary and Shrinithivihahshini, 2017). Additionally, since *L. monocytogenes* has the ability to multiply and grow at low and even freezing temperatures, foods kept in a refrigerator for a long time are the factors for the presence of the pathogen (Kasalica *et al.*, 2011).

Research-based evidence indicates that the prevalence of *L. monocytogenes* has been evident in contaminated raw and pasteurized milk (Mansouri-Najand *et al.*, 2015). However, the investigation of Owusu-Kwarteng *et al.* (2018) showed that the prevalence of *L. monocytogenes* obtained in raw cow milk from the

Table 1 ·The prevalence of *L. monocytogenes* isolates of dairy milk and milk products from different countries

Dairy products	Country	Area	Prevalence (%)	References
Raw milk	Czech republic	–	2.1	Navratilova *et al.*, 2004
	Ethiopia	central high land	2.04	Seyoum *et al.*, 2015
	India	Tiruchengode	16.6	Sreeja *et al.*, 2016
	Turkey	Samsun	5	Kevenk and Terzi Gulel (2016)
	Ghana	Northern Region	8.8	Owusu-Kwarteng *et al.*, 2018
	Iran	Central	7.8	Akrami-Mohajeri *et al.*, 2018
	Ethiopia	Addis Ababa	13	Gebretsadik *et al.*, 2011
	Central Iran	Yazd	7.8	Akrami-Mohajeri *et al.*, 2018
	Iran	Isfahan	4.39	Shamloo *et al.*, 2015
Market milk	India	Kolkata	6.25	Saha *et al.*, 2015
Pasteurized milk	Czech republic	–	5	Navratilova *et al.*, 2004
	Ethiopia	Central high land	20	Seyoum *et al.*, 2015
	India	Tiruchengode	25	Sreeja *et al.*, 2016
Yoghurt	Ethiopia	Central high land	5	Seyoum *et al.*, 2015
Cheese	Ethiopia	Central high land	26.7	Seyoum *et al.*, 2015
	Brazil	Paraná	54.5	Abrahão *et al.*, 2008
Traditional cheese	Central Iran	Yazd	7.5	Akrami-Mohajeri *et al.*, 2018
White cheese	Turkey	Samsun	5	Kevenk and Terzi Gulel (2016)
Farm pooled milk	India	Kolkata	5	Saha *et al.*, 2015
Traditional butter	Central Iran	Yazd	1	Akrami-Mohajeri *et al.*, 2018
Traditional curd	Central Iran	Yazd	1	Akrami-Mohajeri *et al.*, 2018
Dairy product	Turkey	Ankara	10	Şanlıbaba *et al.*, 2018
Traditional ice cream	Central Iran	Yazd	–	Akrami-Mohajeri *et al.*, 2018
Farm cheese	Turkey	Samsun	20	Kevenk and Terzi Gulel (2016)

Northern region of Ghana was 8.8%, whereas no *L. monocytogenes* was detected in boiled cow milk. On the other hand, Navratilova *et al.* (2004) and Sreeja *et al.* (2016) reported higher prevalence of *L. monocytogenes* in pasteurized milk than raw milk as indicated in Table 1. The investigation of Seyoum *et al.* (2015) on different samples of dairy milk collected from the central high land of Ethiopia showed that the prevalence of *L. monocytogenes* varies based on the geographical location (urban areas, 3.4% and peri-urban areas, 1.03%) and the type of samples taken (raw milk, pasteurized milk, yoghurt, and cheese). However, similar to Navratilova *et al.* (2004) and Sreeja *et al.* (2016), this study also obtained higher prevalence of *L. monocytogenes* and pasteurized milk and even in cheese when compared with raw milk and yoghurt (Table 1). The other research work carried out in a total of 415 samples of milk and milk products from Tiruchirappalli city, Tamil Nadu, India confirmed that 219 (52.7%) samples were found *L. monocytogenes* positive. Among these, raw milk and flavoured milk were 100% contaminated by *L. monocytogenes* followed by branded milk (65.9%), cheese (62.5%), ice-cream (49.2%), milk powder (26.6%), milk sweets (20%), ghee and paneer (13.3%), and yoghurt (6.6%), whereas curd and butter were free from *L. monocytogenes* (Mary and Shrinithivihahshini, 2017)

Antibiotic Resistance of Bacteria Isolates of Food Products

Antibiotic resistance is the ability of microorganism to combat the action of one or more antibiotics that are used in clinical practice where the organism changes its response to the antibiotics as reviewed by Olaimat *et al.* (2018). It is a global public health issue, threatens for the effectiveness of antibiotic therapy, and also challenges the efforts for developing new antibiotics. A variety of bacterial pathogens isolated globally have now become multidrug resistance (Li and Nikaido, 2009). In recent years, the food industries have faced a challenge with an emergence of antibiotic-resistant bacterial strains, including pathogens of public health importance such as *Salmonella, Staphylococcus aureus, Escherichia coli*, and *L. monocytogenes* as they potentially cause deterioration of foods. American food supply is among the safest in the world, but people can still get sick from food-borne infections due to antibiotic-resistant bacteria (Centre for Disease Control and Prevention [CDC], NCEZID, 2018).Thus, in USA alone, each year at least 2 million people are infected with antibiotic-resistant bacteria and at least 23,000 people die (Li and Webster, 2018). On similar cases, CDC reported 25,000 annual deaths in the European Union (Sandoiu, 2018) in relation to the effect of antibiotic resistance. It has been the major threats to food security and food development that antibiotic resistance makes the diseases harder to treat as the antibiotics become ineffective, which may increase the mortality rate, the recovery time in hospitals (prolonged hospital stay), as well as medical costs (WHO, 2018a).

Some studies have shown that an extensive use of antibiotics in livestock and poultry feed leads to the formation of antibiotic-resistant bacterial strains, which if they are transmitted to humans through animal products, might cause health problems to consumers (Akrami-Mohajeri *et al.*, 2018). Therefore, antibiotic resistance is also recognized as a challenge to dairy processing industries because of the rapid emergence and spread of resistant bacteria and genes among humans, animals, and environment on a global scale (Rousham *et al.*, 2018). Microorganisms, particularly bacteria, respond differently to antibiotics and other antimicrobial compounds, either due to intrinsic differences or to the development of resistance by adaptation or genetic exchange.

Occurrence and Spread and of Antibiotic Resistance

The use and misuse of antibiotics in farm animal settings as growth promoters or as means of disease treatment has increased antibiotic resistance among bacteria in habitat. This reservoir of resistance may be transferred directly or indirectly to humans through food consumption. The resistant bacteria can cause serious health effects directly or through transmission of antibiotic-resistance traits to pathogens, causing diseases that are difficult to treat (Economou and Gousia, 2015). However, in the review of Phillips *et al.* (2004), it was stated that although antibiotics are used in both animals and humans, most of the resistance problem in humans has arisen from human use. In natural environment, for example, fresh water, the overuse of antibiotics has enhanced the antibiotic resistance, making a potential risk for public health worldwide. In this regard, the antibiotic resistance investigated by Yin *et al.* (2013) in Lake Tailu obtained high percentage of resistance to streptomycin and ampicillin among bacterial isolates, followed by tetracycline and chloramphenicol. Bacterial isolates selected for further study in this area also indicated that some opportunistic pathogens and 62% of the 78 isolates showed multiple antibiotic resistance. The prevalence of antibiotic resistance and the dissemination of transferable antibiotic resistance in bacteria clearly show the urgency of realizing the health risk to human and animals because it becomes a growing global public threat with serious health, political, and economic implications (Devarajan *et al.*, 2016), and as in the review of Olaimat *et al.* (2018), it is also the issue of food security and development because it makes the diseases harder to treat as antibiotics become ineffective.

The antibiotic-resistant bacteria are able to develop the strategic defensive mechanisms to take over the activity of the antibiotics, which may be through transfer of antibiotic-resistant genes to each other or one another by horizontal gene transfer (Figure 1, no. 4). The spread of antibiotic resistance can be carried out through several routes. Person-to-person direct or indirect contact, animals to humans or humans to animals, food, water, and trade are some of the possible routes in which spread of resistant bacteria develops in humans, animals, and environments (Badore, 2013). Poor hygiene and sanitation and poor infection control are interconnected key factors contributing to the spread of resistant bacteria in health care facilities and animal production.

Antibiotic Resistance of *L. monocytogenes* in Dairy Products

The challenge of the pathogenic *L. monocytogenes*, including other food-borne microorganisms, is not limited to only contamination of food items and environment, but also able to resist most commonly known antibiotics that are often used for treatment of infections. Bacterial resistance to antibiotics has been rising dangerously to high level over the world, causing serious public health (WHO, 2018a). The resistance of *L. monocytogenes,* isolates from different dairy products, to some commonly used antibiotics such as penicillin, ampicillin, tetracycline, and gentamicin is evident (Yakubu *et al.*, 2012; Olaimat *et al.*, 2018).The antibiotic resistance of *L. monocytogenes,* which was isolated from 164 samples of three types of dairy-based foods (Baladi cheese, Shankleesh, and Kishk) collected from the Bekaa valley from various sources such as markets, houses, and small family dairy farms in the Northeast regions of Lebanon, was investigated by Harakeh *et al.* (2009) who obtained that more isolates were resistant to oxacillin (93.33%), penicillin (90%), and ampicillin (60%) than to the rest of the antibiotics, indicating the emergence of multidrug-resistant *L. monocytogenes* in the environment. Similarly, the same pathogen isolated from other foods, such as ready-to-eat foods, was found resistant to oxacillin (94.1%) and penicillin (100%), including other antibiotics such as nalidixic acid, ampicillin, linezoid, and lindamycin (Şanlıbaba *et al.*, 2018). Thus, the resistance of such strains to antibiotic drugs would pose a very serious public health problem.

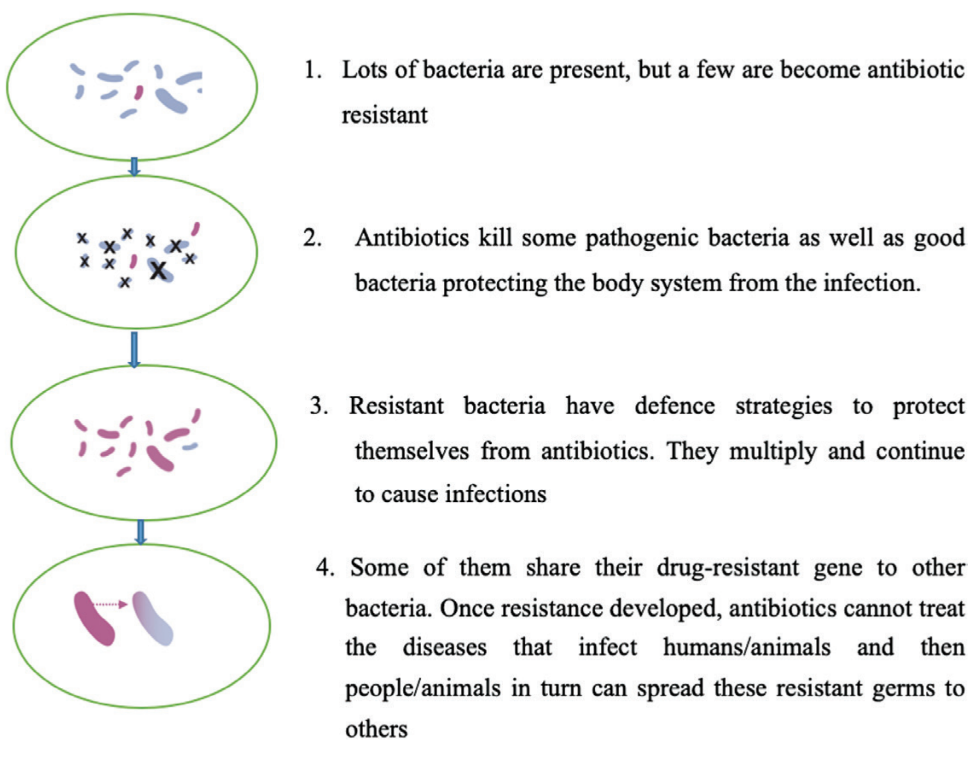

Figure 1. ·Ways of bacterial resistance development. Source: CDC, 2018.

In a study conducted by Girma and Abebe (2018) in bovine raw milk from Debre-Birhan town, Ethiopia, of the total 36 *L. monocytogenes* species subjected for antimicrobial susceptibility test, 11 (30.5%) were resistance to nalidixic acid, followed by 9(25%), 8(22.2%), and 4(11.1%) to tetracycline, chloramphenicol, and streptomicin, respectively. Similarly, according to an investigation done on the antibiotic resistance of *L. monocytogenes* in samples of raw milk and dairy products collected from Samsun, Turkey, among the collected samples, about 15.3% of the isolates were resistant to at least one drug and 36.5% were multidrug-resistant, whereas the most common resistance encountered was to tetracycline (34.6%), followed by chloramphenicol (25%) and penicillin G (23%) (Kevenk and Terzi Gulel, 2016). It is evident that *L. monocytogenes* strains from food products exhibit resistance to other several types of antibiotics, including those of which are frequently used to treat human listeriosis, namely, kanamycin, levofloxacin, amoxicillin, rifampicin, and ciprofloxacin (Şanlıbaba *et al.*, 2018).

Factors Influencing the Antibiotic Resistance of *L. monocytogenes*

Antibiotics are used for different purposes like growth supplements, disease control and prevention, protection of public health, animal production enhancement, and public health associated with antibiotic resistance (Hao *et al.*, 2014). However, when they are misused or extensively used in humans and animals, they greatly contribute to the development and spread of antibiotic resistance among food-borne pathogens including *L. monocytogenes*. The use of antibiotics in low-dose or incomplete courses is the main reason for the emergence and spread of antibiotic resistance. On the other hand, formation of biofilm on foods, instrument, and utensils and lack of new antibiotics being developed can also trigger the ability of the organism to resist the activity of antibiotics. One mechanism of resistance of bacteria is biofilm formation, which is also a mechanism of virulence (Cepas *et al.*, 2019). Biofilm-based infections are extremely difficult to cure because it enhances the resistance of the bacterial strains (Hall and Mah, 2017).

Some food-borne pathogens are naturally resistant to certain antibiotics and this is related to their general physiology, whereas other pathogens develop antibiotic resistance by mutation or other types of genetic alteration (Olaimat *et al.*, 2018). In addition, during their adaptation to environmental stresses, pathogens can become more resistant to antibiotics. *Listeria monocytogenes* may expose to a broad spectrum of sub lethal environmental stresses during food production and processing; this may include physical stressors such as heat, high pressure, desiccation, and irradiation; chemical stressors such as acids, salts, and oxidants; and biological stressors such as microbial antagonism. For pathogenic bacteria, including *L. monocytogenes*, to be resistant to the effect of antibiotics, the following listed in (Table 2) have been found to be the main factors. The bacterial response to stress includes changes in cell composition and physiological state, which enable food-borne pathogens to maintain their normal functions and survive in foods during processing.

Mechanisms and Strategy of Antibiotic Resistance of *L. monocytogenes*

Bacteria constantly find new defence strategies, which is also called 'resistance mechanisms', against the effects of antibiotics (Figure 2). Antibiotic resistance in *L. monocytogenes* is chiefly caused by different genetic mechanisms like self-transferrable plasmids, mobilizable plasmids, and conjugative transposons. However, efflux pumps have also been reported to be linked with antibiotic resistance in *L. monocytogenes* (Navratilova *et al.*, 2004). Transmission of resistance among bacterial species has been demonstrated. The transmission from *L. monocytogenes* to *S. aureus*, and from *Escherichia coli* to *S. aureus* and *L. monocytogenes* by *Enterococci* and *streptococci*, in particular, represent a reservoir of genes of resistance for *L. monocytogenes*. The resistance mechanisms are developed by using instructions provided by their DNA. Resistance genes are often found within plasmids, small pieces of DNA that carry genetic instructions from one to another. Thus, the transferability of antibiotic resistance genes among bacteria enables further spread of antibiotic-resistant bacteria (Bertsch *et al.*, 2014).

Antibiotic Resistance Mediated by Conjugation

Conjugation is the process of transfer of genetic materials between bacterial cells by direct cell to cell or by bridge like connection between two cells. It takes place when the genetic materials transfer from the donor to the recipient cells like streptomycin-resistant *L. monocytogenes* LM35 (donor) and streptomycin-sensitive *L. monocytogenes* LM65 and LM100 (recipient strains) (Purwati *et al.*, 2001). The investigation of Pourshaban *et al.*, (2002) on transferrable tetracycline resistance in *L. monocytogenes* isolates

Table 2 Antibiotic resistance of *L. monocytogenes* (isolates of dairy milk and milk products) to some selected antibiotics in different countries

Antibiotics	Countries				
	Central Iran	Nigeria	Ethiopia	India	Turkey
	(Yazd)	(Sokoto)	(Debre Birhan)	(Kolkata)	(Samsun)
Tetracycline	86.3%	0%	25%	0%	34.6%
Chloramphenicol	77.2%	0%	22.2%	40%	25%
Ampicillin	–	100%	–	0%	9.6%
Penicillin G	77.2%	–	–	0%	23%
Gentamicin	18.1%	10%	–	0%	–
Erythromycin	36.3%	–	–	–	9.6%
Streptomycin	45.5%	20%	11.1%	–	–
Ciprofloxacin	–	0%	–	100%	–
References	Akrami-Mohajeri *et al.*, 2018	Yakubu *et al.*, 2012	Girma and Abebe, 2018	Saha *et al.*, 2015	Kevenk and Terzi Gulel (2016)

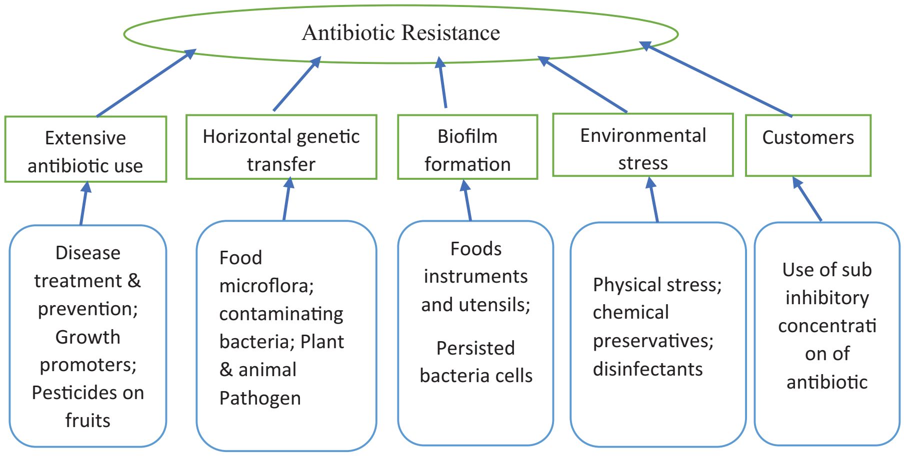

Figure 2. ·Factors influencing antibiotic resistance of *Listeria monocytogenes*. Source: Malekmohammadi *et al.*, 2017; Olaimat *et al.*, 2018.

of foods indicated that *L. monocytogenes* stains 266 and 286 and *L. innocua* 52P transferred tetracycline resistance to *L. ivanovii* through conjugation, whereas only *L. monocytogenes* and *L. innocua* 52P transferred resistance to *Enterococcus faecalis*. The genome of bacteria is composed of the chromosome and accessory movable genetic elements such as transposons and plasmids. In this process of transfer, the genetic materials can be transferred from one cell to another; for example, *Streptococcus agalactiae*, which its plasmid is resistant to antibiotics such as chloramphenicol and macrolides, and *Enterococcus*, which is resistant to erythromycin, both can be transferred to *Listeria monocytogenes*.

In gastrointestinal tract of animals and in food processing plants, *L. monocytogenes* can be exposed to conjugation with *Entrococcus* species and *Staphylococcus* species carrying plasmids coding for antibiotic resistance. On the other hand, the gut of some insects, like cockroaches, thought as an effective in vivo model for the natural transfer of antimicrobial resistance plasmids among bacteria, playing a crucial role in conjugation-mediated genetic exchanges. Regarding this, a study evaluated a conjugation-mediated horizontal transfer of resistance genes between *Escherichia coli* and other organisms of the same family within the intestine of Blaberus craniifer Burmeister revealed that the insects allow for the exchange of antimicrobial resistance plasmids among bacteria and may signify a potential reservoir for the dissemination of antibiotic-resistant bacteria in different environments (Anacarso *et al.*, 2016).

Antibiotic Resistance Mediated by Efflux Pumps

Efflux pumps are membrane proteins found in both Gram-positive and Gram-negative bacteria that are involved in detoxifying cells, including antibiotics, from within cells to the external environment (Lungu *et al.*, 2011). They export antibiotics from the cell and maintain their low-intracellular concentrations and also determine the intrinsic and/or acquired resistance (Poole, 2005).They have also been considered as one of the mechanisms responsible for the antimicrobial resistance in biofilm-forming microorganisms such as *Listeria monocytogenes*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Candida albicans* (Soto, 2013).

Two groups of *L. monocytogenes* strains, strains naturally sensitive to benzalkonium chloride and strains naturally resistant to benzalkonium chloride, were studied by Romanova *et al.* (2006) to investigate potential mechanisms underlying resistance and sensitive to benzalkonium chloride in *L. monocytogenes*. In this study, reserpine, an efflux pump inhibitor, was added to the strains to investigate the role of efflux pumps in sensitivity/adaptation or resistance, resulting in a decrease in minimum inhibition concentration for benzalkonium chloride, whereas no decrease was observed for resistant strains, indicating that efflux pumps played no role in innate resistance of certain strains of *L. monocytogenes* to this compound. The pumps may be specific for one substrate or may transport a range of structurally dissimilar compounds, including antibiotics of multiple classes; such pumps can be associated with multiple drug resistance, as reviewed by Webber and Piddock (2003). Bacterial efflux pumps have evolved as a protective mechanism in both Gram negative and Gram positive, and particularly Gram-negative bacteria to maintain cell homeostasis and communication by actively pumping out solutes, metabolites, quorum sensing molecules, and toxins, especially antimicrobial compounds. They can be specific to antibiotics. However, most of them are multidrug transporters that are capable of pumping a wide range of unrelated antibiotics like macrolides and tetracycline and thus significantly contribute to multidrug-resistant organisms and Sun *et al.* (2014) also reviewed on the mechanism, physiology, and pharmacological exploitation of efflux pump inhibitors as promising antidrug resistance interventions.

Modification or Change of the Target Molecule

Natural variations or acquired changes in the target sites of antibiotics that prevent drug binding are a common mechanism of resistance. Target site changes often result from spontaneous mutation of a bacterial gene on the chromosome. Bacterial resistance is always caused by molecular changes at the bacterial surfaces, which alter the nature of specific drug-target interactions (Ndieyira *et al.*, 2017). Since antibiotic interaction with target molecule is generally quite specific, minor alteration of the target molecule can have an important effect on the antibiotic binding. When antibiotics are designed to single out and destroy specific part of the bacterium, the resistant bacterium can change the look of their targets so that the antibiotics cannot recognize and destroy them, allowing the bacteria to survive. Therefore, modifying the target on which antibiotics bind and act is another mechanism of developing bacterial resistance against antibiotics (Kapoor *et al.*, 2017). For example, when the structure of penicillin binding protein (PBP) in bacteria is altered, penicillin can no longer bind to that protein and it becomes ineffective.

Membrane Fluidity

Membrane fluidity can play an important role in antimicrobial resistance of *L. monocytogenes*. The sensitivity of *L. monocytogenes* to antimicrobial compounds was altered when bacterial membrane lipid composition was modified by growth in the presence of added fatty acids. The cells of *L. monocytogenes* grown in the presence of carbon chain (C14:0 or C18:0) of fatty acids have higher phase transition and increased resistance to antibiotics than cells grown in the presence of carbon chain (C18:1) of fatty acyl (Juneja and Davidson, 1993). *Listeria monocytogenes* has high levels of branched-chain fatty acids. This leads to maintenance of constant membrane fluidity at low temperatures by including fatty acids with lower phase-transition temperatures (Kapoor *et al.*, 2017). The fluidity of membrane lipid bilayer is altered mainly through the adjustment of membrane fatty acid composition. *Listeria monocytogenes* strains typically alter their membrane fluidity with changes in fatty acid chain length or by forming branched-chain fatty acids (Yoon *et al.*, 2015). Branched-chain fatty acids represent the dominant group of membrane fatty acids and have been established as crucial determinants in *L. monocytogenes* resistance ability. This mechanism is mediated by membrane fluidity by modulating membrane fatty acid composition.

Quorum Sensing in Biofilm Formation

Listeria monocytogenes strains possess a strong biofilm-forming capability which poses a great challenge to the food industry because of its inherent resistance to the action of disinfectants (Olaimat *et al.*, 2018). Bacterial cell to cell inter-communication system through coordinated chemical signalling has played a vital role in biofilm formation and shaping of the biofilm in food-borne microorganisms such as *L. monocytogenes* (Toyofuku *et al.*, 2016).The bacteria inducing a particular set of genes are capable of sensing and responding to increased cell population density. Genetic materials expression in some bacterial species may be regulated by the system of stimulus called quorum sensing, which enhance the resistance ability of the organism (Annous *et al.*, 2009).

Quorum sensing includes the production and secretion of acyl homoserine lactones, which diffuse through the cell wall from the cell to the medium. In Gram-positive bacteria, quorum sensing secretes peptides as signal compounds and a two regulatory system (membrane-bound histidine kinase receptor and an intracellular response regulator) to detect the required changes in gene expression pattern and the peptides (Singh *et al.*, 2017). It uses signalling molecules, auto inducers, which are frequently produced by bacteria mainly at the stage of micro-colony formation (Zhao *et al.*, 2017) and easily diffuse throughout the cell membrane where the concentration of signalling molecules becomes higher following the larger number of bacteria present around the area. After the concentration of signalling reaches a threshold level, it is recognized by receptors found in the cytoplasm or cell membrane and activates gene expression involved in signal production (Mansouri-Najand *et al.*, 2015).

Conclusions and Recommendations

Listeria monocytogenes is the bacterial pathogen mostly common in causing food-borne infections by contaminating food items. The presence of the pathogen in dairy products has imposed a serious public health globally. Foods kept in the refrigeration more than the prescribed time create an opportunity for the occurrence of *Listeria monocytogenes*. The prevalence of *L. monocytogenes* isolates of dairy products has been commonly challenging the dairy processing industry; since the organism has the ability to develop biofilm, the standard cleaning and disinfections, routinely applied, may not be fully effective in eliminating it. The pathogen has also the ability to resist the activity of most commonly used antibiotics. The antibiotic resistance of *L. monocytogenes* isolates of dairy products is another concern of health issue because the antibiotic resistance of the microorganism has been developed against the activity of the antibiotics. Based on the review, preventive measures, including good hygienic and sanitation practice in dairy products, good dairy management, and quality feed supply, are more practical for keeping food safety and quality.

Conflict of interest statement. The authors certify that there are no conflicts of interest with any organization, financial, or other regarding the material discussed in the manuscript.

References

Abrahão, W. M., da Silva Abrahão, P. R., Monteiro, C. L. B., Pontarolo, R. (2008). Ocorrência de *Listeria monocytogenes* em queijos e sorvetes produzidos no Estado do Paraná, Brasil. *Revista Brasileira de Ciências Farmacêuticas*, 44(2): 289–296.

Akrami-Mohajeri, F., Derakhshan, Z., Ferrante, M., Hamidiyan, N., Soleymani, M., Conti, G. O., Tafti, R. D. (2018). The prevalence and antimicrobial resistance of *Listeria* spp in raw milk and traditional dairy products delivered in Yazd, central Iran (2016). *Food and Chemical Toxicology,* 114: 141–144.

Anacarso, I., Iseppi, R., Sabia, C., Messi, P., Condò, C., Bondi, M., De Niederhäusern, S. (2016). Conjugation-mediated transfer of antibiotic-resistance plasmids between enterobacteriaceae in the digestive tract of *Blaberus craniifer* (Blattodea: Blaberidae). *Journal of Medical Entomology,* 53: 591–597.

Andersson, C., Gripenland, J., Johansson, J. (2015). Using the chicken embryo to assess virulence of *Listeria monocytogenes* and to model other microbial infections. *Nature Protocols,* 10: 1155–1164.

Annous, B. A., Fratamico, P. M., Smith, J. L. (2009). Scientific status summary. *Journal of Food Science,* 74: R24–R37.

Badore, M. (2013). *New CDC Report Links Factory Farms to Antibiotic Resistance (Infographic)*. Center for Disease Control and Prevention (CDC). https://www.treehugger.com/sustainable-agriculture/new-cdc-report-links-factory-farms-antibiotic-resistance.html (Accessed 21 August 2019).

Bangieva, D., Rusev, V. (2017). Prevalence of *Listeria monocytogenes* in raw cow milk–a review. *Bulgarian Journal of Veterinary Medicine*, 20(1): 430–436.

Bertsch, D., Muelli, M., Weller, M., Uruty, A., Lacroix, C., Meile, L. (2014). Antimicrobial susceptibility and antibiotic resistance gene transfer analysis of foodborne, clinical, and environmental *Listeria* spp. isolates including *Listeria monocytogenes*. *Microbiologyopen*, 3: 118–127.

Center for Food Safety, CFS. (2014). Potential Risk of Listeria in Refrigerated Foods with Long Shelflife. 17 September 2014.

Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID). (2018). Antibiotic/Antimicrobial Resistance AR/AMR. 10 September 2018. https://www.cdc.gov/drugresistance/about.html (Accessed 21 August 2019).

Centorame, P., D'Angelo, A. R., Di Simone, F., Salini, R., Cornacchia, A., Marrone, R., Pomilio, F. (2017). *Listeria monocytogenes* biofilm production on food packaging materials submitted to physical treatment. *Italian Journal of Food Safety*, 6: 6654.

Cepas, V., López, Y., Muñoz, E., Rolo, D., Ardanuy, C., Martí, S., Soto, S. M. (2019). Relationship between biofilm formation and antimicrobial resistance in gram-negative bacteria. *Microbial Drug Resistance (Larchmont, N.Y.)*, 25: 72–79.

Cossart, P. (2011). Illuminating the landscape of host–pathogen interactions with the bacterium *Listeria monocytogenes*. *Proceedings of the National Academy of Sciences, United States of America*, 108(49): 19484–19491.

Devarajan, N., Laffite, A., Mulaji, C. K., Otamonga, J. P., Mpiana, P. T.,Mubedi, J. I., Poté, J. T.. (2016). Occurrence of antibiotic resistance genes and bacterial markers in a tropical river receiving hospital and urban wastewaters. *Plos One*, 11: e0149211.

Economou, V., Gousia, P. (2015). Agriculture and food animals as a source of antimicrobial-resistant bacteria. *Infection and Drug Resistance*, 8: 49–61.

Gebretsadik, S., Kassa, T., Alemayehu, H., Huruy, K., Kebede, N. (2011). Isolation and characterization of *Listeria monocytogenes* and other *Listeria* species in foods of animal origin in Addis Ababa, Ethiopia. *Journal of Infection and Public Health*, 4: 22–29.

Girma Y., Abebe B. (2018). Isolation, identification and antimicrobial susceptibility of *Listeria* species from raw bovine milk in Debre-Birhan Town, Ethiopia. *Journal of Zoonotic Diseases and Public Health*; 2(1):4.

Hall, C. W., Mah, T. F. (2017). Molecular mechanisms of biofilm-based antibiotic resistance and tolerance in pathogenic bacteria. *FEMS Microbiology Reviews*, 41: 276–301.

Hao, H., Cheng, G., Iqbal, Z., Ai, X., Hussain, H. I., Huang, L., Yuan, Z. (2014). Benefits and risks of antimicrobial use in food-producing animals. *Frontiers in Microbiology*, 5: 288.

Harakeh, S., Saleh, I., Zouhairi, O., Baydoun, E., Barbour, E., Alwan, N. (2009). Antimicrobial resistance of *Listeria monocytogenes* isolated from dairy-based food products. *The Science of the Total Environment*, 407: 4022–4027.

Hunt, K., Drummond, N., Murphy, M., Butler, F., Buckley, J., Jordan, K. (2012). A case of bovine raw milk contamination with *Listeria monocytogenes*. *Irish Veterinary Journal,* 65: 13.

Juneja, V. K., Davidson, P. M. (1993). Influence of altered fatty acid composition on resistance of *Listeria monocytogenes* to antimicrobials. *Journal of Food Protection,* 56: 302–305.

Kapoor, G., Saigal, S., Elongavan, A. (2017). Action and resistance mechanisms of antibiotics: a guide for clinicians. *Journal of Anaesthesiology, Clinical Pharmacology*, 33: 300–305.

Kasalica, A., Vuković, V., Vranješ, A., Memiši, N. (2011). *Listeria monocytogenes* in milk and dairy products. *Biotechnology in Animal Husbandry*, 27(3): 1067–1082.

Kevenk, T. O., Terzi Gulel, G. (2016). Prevalence, antimicrobial resistance and serotype distribution of *Listeria monocytogenes* isolated from raw milk and dairy products. *Journal of Food Safety*, 36(1): 11–18.

Lee, S. H. I., Cappato, L. P., Guimarães, J. T., Balthazar, C. F., Rocha, R. S., Franco, L. T., de Oliveira, C. A. F. (2019). *Listeria monocytogenes* in milk: occurrence and recent advances in methods for inactivation. *Beverages*, 5(1): 14.

Leong, W. M., Geier, R., Engstrom, S., Ingham, S., Ingham, B., Smukowski, M. (2014). Growth of *Listeria monocytogenes*, *Salmonella* spp., *Escherichia coli* O157:H7, and *Staphylococcus aureus* on cheese during extended storage at 25°C. *Journal of Food Protection*, 77: 1275–1288.

Li, X. Z., Nikaido, H. (2009). Efflux-mediated drug resistance in bacteria: an update. *Drugs*, 69: 1555–1623.

Li, B., Webster, T. J. (2018). Bacteria antibiotic resistance: new challenges and opportunities for implant-associated orthopedic infections. *Journal of Orthopaedic Research*, 36: 22–32.

Lopez-Valladares, G., Danielsson-Tham, M. L., Tham, W. (2018). Implicated food products for listeriosis and changes in serovars of *Listeria monocytogenes* affecting humans in recent decades. *Foodborne Pathogens and Disease*, 15: 387–397.

Lungu, B., O'Bryan, C. A., Muthaiyan, A., Milillo, S. R., Johnson, M. G., Crandall, P. G. M., Ricke, S. C. (2011). *Listeria monocytogenes*: antibiotic resistance in food production. *Foodborne Pathogens and Disease*, 8: 569–578.

Malekmohammadi, S., Kodjovi, K. K., Sherwood, J., Bergholz, T. M. (2017). Genetic and environmental factors influence *Listeria monocytogenes* nisin resistance. *Journal of Applied Microbiology*, 123: 262–270.

Mansouri-Najand, L., Kianpour, M., Sami, M., Jajarmi, M. (2015). Prevalence of *Listeria monocytogenes* in raw milk in Kerman, Iran. *Veterinary Research Forum*, 6: 223–226.

Martinović, T., Andjelković, U., Gajdošik, M. Š., Rešetar, D., Josić, D. (2016). Foodborne pathogens and their toxins. *Journal of Proteomics*, 147: 226–235.

Mary, M. S., Shrinithivihahshini, N. D. (2017). Pervasiveness of *Listeria monocytogenes* in milk and dairy products. *Journal of Food: Microbiology, Safety, and Hygiene*, 2(125): 2476–2059.

Navratilova, P., Schlegelova, J., Sustackova, A., Napravnikova, E., Lukasova, J., Klimova, E. (2004). Prevalence of *Listeria monocytogenes* in milk, meat and foodstuff of animal origin and the phenotype of antibiotic resistance of isolated strains. *Veterinary Medicine*, 49 (7): 243–252.

Ndieyira , J. W., Bailey, J., Patil, S. B., Vögtli, M., Cooper, M. A., Abell, C., Aeppli, G. (2017). Surface mediated cooperative interactions of drugs enhance mechanical forces for antibiotic action. *Scientific Reports,* 7: 41206.

Olaimat, A. N., Al-Holy, M. A., Shahbaz, H. M., Al-Nabulsi, A. A., Abu Ghoush, M. H., Osaili, T. M., Holley, R. A. (2018). Emergence of antibiotic resistance in listeria monocytogenes isolated from food products: a comprehensive review. *Comprehensive Reviews in Food Science and Food Safety*, 17(5): 1277–1292.

Owusu-Kwarteng, J., Wuni, A., Akabanda, F., Jespersen, L. (2018). Prevalence and characteristics of *Listeria monocytogenes* isolates in raw milk, heated milk and nunu, a spontaneously fermented milk beverage, in Ghana. *Beverages*, 4(2): 40.

Pantoja, J. C. F., Rodrigues, A. C. O., Hulland, C., Reinemann, D. J., Ruegg, P. L. (2012). Investigating contamination of bulk tank milk with *Listeria monocytogenes* on a dairy farm. *Food Protection Trends*, 32(5): 512–521.

Phillips, I., Casewell, M., Cox, T., De Groot, B., Friis, C., Jones, R., Waddell, J. (2004). Does the use of antibiotics in food animals pose a risk to human health? A critical review of published data. *The Journal of Antimicrobial Chemotherapy*, 53: 28–52.

Pitt, W. M., Harden, T. J., Hull, R. R. (2000). Behavior of *Listeria monocytogenes* in pasteurized milk during fermentation with lactic acid bacteria. *Journal of Food Protection*, 63: 916–920.

Poole, K. (2005). Efflux-mediated antimicrobial resistance. *The Journal of Antimicrobial Chemotherapy,* 56: 20–51.

Pourshaban, M., Ferrini, A. M., Mannoni, V., Oliva, B., Aureli, P. (2002). Transferable tetracycline resistance in *Listeria monocytogenes* from food in Italy. *Journal of Medical Microbiology*, 51: 564–566.

Purwati, E., Radu, S., Hassan, Z., Ling, O. W., Rahim, R. A. (2001). Plasmid-mediated streptomycin resistance of *Listeria monocytogenes*. *The Malaysian Journal of Medical Sciences*, 8: 59–62.

Rahimi, E., Momtaz, H., Sharifzadeh, A., Behzadnia, A., Ashtari, M. S., Esfahani, S. Z., Momeni, M. (2012). Prevalence and antimicrobial resistance of *Listeria* species isolated from traditional dairy products in Chahar Mahal & Bakhtiyari, Iran. *Bulgarian Journal of Veterinary Medicine*, 15(2): 115–122.

Ramaswarmy, V., Cresence, V. M., Rejitha, J. S., Lekshmi, M. U., Dharsana, K. S., Prasad, S. P. (2007). *Listeria*–review of epidemiology and pathogenesis. *Journal of Microbiology, Immunology, and Infection = Wei Mian Yu Gan Ran Za Zhi*, 40: 4–13.

Romanova, N. A., Wolffs, P. F., Brovko, L. Y., Griffiths, M. W. (2006). Role of efflux pumps in adaptation and resistance of *Listeria monocytogenes* to benzalkonium chloride. *Applied and Environmental Microbiology,* 72: 3498–3503.

Rousham, E. K., Unicomb, L., Islam, M. A. (2018). Human, animal and environmental contributors to antibiotic resistance in low-resource settings: integrating behavioural, epidemiological and One Health approaches. *Proceedings of the Royal Society B: Biological Sciences*, 285(1876): 20180332.

Saha, M., Debnath, C., Pramanik, A. k., Murmu, D., Kumar, R., Mitra, T. (2015). Studies on the prevalence of *Listeria Monocytogenes* in unpasteurized raw milk intended for human consumption in and around Kolkata, India. *International Journal of Current Microbiology and Applied Science*, 4(8): 288–298.

Sandoiu, A. (2018). Drug resistance: does antibiotic use in animals affect human health? Newspaper, Medical News Today. Friday 9 November 2018. https://www.medicalnewstoday.com/articles/323639.php. (Accessed 21 August 2019).

Şanlıbaba, P., Tezel, B. U., Çakmak, G. A. (2018). Prevalence and antibiotic resistance of *Listeria monocytogenes* isolated from ready-to-eat foods in Turkey. *Journal of Food Quality*, 2018: 9.

Seyoum, E. T., Woldetsadik, D. A., Mekonen, T. K., Gezahegn, H. A., Gebreyes, W. A. (2015). Prevalence of *Listeria monocytogenes* in raw bovine milk and milk products from central highlands of Ethiopia. *Journal of Infection in Developing Countries,* 9: 1204–1209.

Shamloo, E., Jalali, M., Mirlohi, M., Madani, G., Metcalf, D., Merasi, M. R. (2015). Prevalence of *Listeria* species in raw milk and traditional dairy products in Isfahan, Iran. *International Journal of Environmental Health Engineering*, 4(1), 1.

Singh, S., Singh, S. K., Chowdhury, I., Singh, R. (2017). Understanding the mechanism of bacterial biofilms resistance to antimicrobial agents. *The Open Microbiology Journal*, 11: 53–62.

Soto, S. M. (2013). Role of efflux pumps in the antibiotic resistance of bacteria embedded in a biofilm. *Virulence*, 4: 223–229.

Sreeja, S., Moorthy, K., Vivek, N. Upasani (2016). Prevalence of *Listeria monocytogenes* in raw and pasteurized milk samples from Tiruchengode (TN), India. *International Journal of Innovative Research in Science, Engineering and Technology*, 5(2): 1419–1424.

Sun, J., Deng, Z., Yan, A. (2014). Bacterial multidrug efflux pumps: mechanisms, physiology and pharmacological exploitations. *Biochemical and Biophysical Research Communications*, 453: 254–267.

Toyofuku, M., Inaba, T., Kiyokawa, T., Obana, N., Yawata, Y., Nomura, N. (2016). Environmental factors that shape biofilm formation. *Bioscience, Biotechnology, and Biochemistry*, 80: 7–12.

Webber, M. A., Piddock, L. J. (2003). The importance of efflux pumps in bacterial antibiotic resistance. *The Journal of Antimicrobial Chemotherapy*, 51: 9–11.

World health Organization, WHO. (2003). *WHO Country Cooperation Strategy 2003–2006 Vietnam*. Ha Noi: WHO.

World health Organization, WHO. (2018a). Antibiotic resistance, 5, February 2018. https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance (Accessed 21 August 2019).

World health Organization, WHO. (2018b). Listeriosis, 20 February, 2018. https://www.who.int/news-room/fact-sheets/detail/listeriosis (Accessed 21 August 2019).

Yakubu, Y., Salihu, M. D., Faleke, O. O., Abubakar, M. B., Junaidu, A. U., Magaji, A. A., Aliyu, R. M. (2012). Prevalence and antibiotic susceptibility of *Listeria monocytogenes* in raw milk from cattle herds within Sokoto Metropolis, Nigeria. *Sokoto Journal of Veterinary Sciences*, 10(2): 13–17.

Yin, Q., Yue, D., Peng, Y., Liu, Y., Xiao, L. (2013). Occurrence and distribution of antibiotic-resistant bacteria and transfer of resistance genes in Lake Taihu. *Microbes and Environments*, 28: 479–486.

Yoon, Y., Lee, H., Lee, S., Kim, S., Choi, K. H. (2015). Membrane fluidity-related adaptive response mechanisms of foodborne bacterial pathogens under environmental stresses. *Food Research International*, 72: 25–36.

Zhao, X., Zhao, F., Wang, J., Zhong, N. (2017). Biofilm formation and control strategies of foodborne pathogens: food safety perspectives. *RSC Advances*, 7(58): 36670–36683.