Antibiotic-resistant bacteria in milk and some dairy products

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Milk and dairy products have an essential role in the diet regarding their mineral content, protein components and vitamins. Antibiotic has been used for treatment and feeding additives in food animals for many years. In 2001, the European Commission launched an investigation about use of antibiotics in farm animals. The EU and our country banned the use of antibiotics as growth promoters in animal feed except for poultry on January 1, 2006. The researchers reported that excessive and misuse of antibiotics lead to resistance of some bacteria in the animals and the environment. Nowadays, antibiotic-resistant bacteria have become a global threat. The incidence of these bacteria which have spread by a variety of ways such as personnel, animal, waste, soil, and water are increasing. Moreover, the final food products could be contaminated by the resistant bacteria. As a result of contaminated food, the resistant bacteria could transfer to human by consumption.

Keywords: milk, dairy product; antibiotic resistance, food-producing animal

1. Introduction

In 1928, Alexander Fleming accidentally discovered the first antibiotic penicillin from the fungus *Penicillium notatum* in a *Staphylococcus* culture plate, despite the antibacterial properties of mold had been known since ancient times. Then to be the first sulfonamide, prontosil was synthesised against streptococcus infections in 1935 by Gerhard Domagk. Moreover, the antibiotic discoveries continued in the following years [1]. A. Fleming, in Nobel Prize speech at 1945 had warned that bacteria could become resistant to these remarkable drugs [2, 3].These drugs have used extensively, inappropriately in both humans and veterinary medicine over several decades [4]. Consequently, today we confront with warnings of A. Fleming. Microorganisms have developed resistance mechanisms against antibiotics within less than one year to more than ten years after the advent of every antimicrobial drug [5]. The term "antibiotic" that was the first used in 1942 by Selman Waksman has limited meaning than "antimicrobial. While antibiotic is a bactericidal or bacteriostatic agent, antimicrobial includes substances that act against all microorganisms such as, bacteria, viruses, parasites, and fungi. At present World Health Organization (WHO), European Food Safety Authority (EFSA) and another organization use antimicrobial resistance (AMR) including antibacterial resistance (ABR) [2]. Same antimicrobials or which belong to the same class are widely used in human and veterinary medicine to treat infectious diseases. This situation resulted in increased AMR. Today, AMR is a global health threat due to the fact that is treatment becoming more difficult or even impossible to current antibiotics, causing higher morbidity and mortality and burdening huge costs [6, 7, 8, 2]. After the usage of antimicrobials in animals for disease treatment, prevention, control, and growth promotion (AGPs), feed efficiency, many researchers studied links between antimicrobial usage in animals with the presence of AMR bacteria at humans. In the mid-1950s, microbiologists and infectious disease experts were firstly faced with the fact that workers and animals of the farms that use antibiotics as AGP have much more resistant bacteria in their intestinal flora than those in non-using [7].

WHO was first expressed that AMR pathogens could be transmitted to humans via the food chain due to the use of antimicrobials in livestock production in 1997. After, the emergence of quinolone-resistant enteric bacteria, WHO met in council about the use of quinolones in food-producing animals in Geneva, in June 1998 [2]. In 2001, the European Commission launched an investigation to use of antibiotics in farm animals. In the directive 2003 states that *the alarming emergence of resistance to antimicrobial agents such as antimicrobial medicinal products and antimicrobial feed additives, besides, not only zoonotic agents but also another indicator organisms might be monitored.* Moreover, many European Union (EU) member states have ensured the monitoring of the use of antimicrobial agents in both human and veterinary medicine before the adaption of the Directive 2003/99/EC [4]. Since AMR problem requires a multidisciplinary approach, the Executive Committee of the Codex Alimentarius Commission recommended that Food and Agriculture Organization of the United Nations (FAO), World Organisation for Animal Health (OIE) and WHO discuss this global health problem at the joint meeting. FAO, OIE, WHO were initiated to study on non-human antimicrobial usage and AMR on December 2003 in Geneva. Finally, the EU and Turkey banned the use of antibiotics as growth promoters in animal feed except for poultry on January 1, 2006 [9, 10]. In the United States, Canada, Russia, China, India, New Zealand, Australia and Brazil, the use of antibiotics as feed additives is still allowed to be used in quantities specified in the regulations [8, 9, 10]. Nowadays, although "One Health" approach describes has been recognized since the 1800s, many professionals who are studying in a different field such as public health, animal health, plant health and the environment have adopted. Many of the same microorganisms infect human and animals because they live and share the same eco-systems. To eliminate the AMR problem, many organization and different professionals should work together under the "One Health" approach. "One Health" approach is a principle to describe that human and animal health are interconnected also encompasses the environment was expanded and became a movement by public health and animal health communities in the EU and in the 2016 United Nations Political Declaration on AMR [11, 12].

2. Milk and dairy production in the EU and Turkey

In the Western world, the use of plant-based milk substitutes such as soy, rice, oats or almonds has increased steadily. However, the Danish Veterinary and Food Administration and the Swedish National Food Agency have stated that plant-based beverages cannot be offered as an alternative to bovine milk regarding nutrients [13]. Also, Milk and dairy products are the most important source of nutrients including calcium and vitamin D particularly for children and adolescents [14]. Demands for milk and dairy product are growing all over the world, despite changes in consumers diets. World milk production reached 833.5 million tonnes in 2017. Consequently, milk and its products are a vital food in human life. Hence researchers have focused on favourable or adverse effects that occurred with consuming milk and dairy products [15]. Milk and dairy product has an important role in the diet regarding their mineral content, protein components and vitamins. 53 % of the raw milk produced is delivered to the dairies in the world; this rate is 94% in the European Union. In 2016, while the farms produced approximately 163.0 million tonnes of cattle milk in the EU-28, 157.1 million tonnes of milk produced was delivered to the dairies to process into some fresh and manufactured products [16]. According to data of the Turkish Statistical Institute in 2016, 16.7 million tonnes of raw milk was produced in Turkey [17]. The processing of the raw milk at the industry is below these rates, and the remaining amount is used on the farms, i.e. processed, own-consumed, sold directly to the consumer, or used as feed. Milk and dairy production rates in EU and Turkey were given in Table 1. The foods, especially foods from animals, are one of the most common vectors for the spread of AMR [18]. For example, in 1985, Scientists showed that an outbreak of multidrug-resistant *Salmonella enterica* serovar, in Arizona which caused the death of a 72-year-old woman, related to consumption of raw milk. Isolates obtained from patients and milk had the same resistance plasmid [7].

Table 1 Collection of milk by dairies and dairy products obtained from milk, 2016 (1 000 tonnes).

	Milk collected from cows	Milk obtained from other animals	Drinking milk	Cream for direct consumption	Milk powder	Butter	Cheese
EU-28	153 195	3 730	30 700	2 770	2 800	2 400	9 616
Belgium	3 882	56	689	234	208	58	110
Bulgaria	524	36	67	2	0	1	80
Czech Republic	2 793	0	616	57	39	28	142
Denmark	5 364	0	519	72	129	110	369
Germany	31 973	15	4 843	587	694	507	1 863
Estonia	715	0	99	26	2	5	43
Ireland	6 851	0	543	25	:	:	205
Greece	602	748	414	13	0	1	204
Spain	6 881	970	3 406	107	46	46	461
France	24 553	777	3 395	460	508	434	1 920
Croatia	490	7	293	29	:	4	36
Italy	11 490	656	2 428	131	:	95	1 232
Cyprus	198	52	65	3	0	0	27
Latvia	814	0	62	36	:	7	39
Lithuania	1 416	0	93	23	36	18	98
Luxembourg	362	0	:	:	0	:	:
Hungary	1 547	0	513	6	:	8	80
Malta	43	0	:	:	0	0	:
Netherlands	14 324	289	557	:	355	232	911
Austria	3 098	16	794	75	12	34	195
Poland	11 140	2	1 655	258	180	204	806
Portugal	1 849	46	710	20	27	31	75
Romania	952	52	278	70	2	12	88
Slovenia	575	0	157	12	:	2	15
Slovakia	823	7	251	31	4	9	38
Finland	2 390	0	673	61	:	64	84
Sweden	2 862	0	785	113	82	61	87
United Kingdom	14 684	0	6 746	296	113	135	404
Norway	1 572	22	:	:	:	:	:
Switzerland	3 407	0	421	24	11	20	100
Serbia	845	1	451	87	103	48	185
Turkey	9 214	91	1 434	32	124	58	658

: not available [1] Eurostat estimates [16]

3. Usage of antibiotics in a dairy farm and antibiotic-resistant bacteria

While the antimicrobials were first introduced to control bacterial infections in humans in the early 1940s, they were used in food-producing and companion animals in veterinary medicine in the 1950s. Also, antimicrobials are used in fish farming, and plants to control some diseases [19]. In the food-producing animal, antibiotics are mainly used to treat clinical cases, to prevent, to control common disease and also, to raise animal growth. These usages have been described as therapeutic use, prophylactic use, and subtherapeutic use. Antibiotics can be applied to a single animal to treat a clinical disease, as well as a group of animals for defence [20]. For example, mastitis that presents clinically or subclinically is one of the most critical and costly infectious diseases in the dairy farms [21, 22]. The rate of clinical mastitis changes from 45 to 65 cases per 100 cows in dairy herds in the United Kingdom, 30 to 35 cases per 100 cows in Japan, 10 to 30 cases per 100 cows in North America, Europe, and New Zealand [23, 24]. Antibiotics such as cefquinom (fourth generation cephalosporin) used to treat mastitis infection also they could be used for the prevention of infection ceftiofur (3rd generation cephalosporin), cephalexin (1st generation cephalosporin), oxytetracycline, penicillins, aminoglycosides and aminocoumarin antibiotics have been used for the treatment of the other bacterial infections of dairy cattle in the farm [25]. 16% of all lactating dairy cattle get antibiotic therapy against mastitis every year, also almost all dairy cattle get protective doses of antibiotics to prevent and control mastitis diseases. In the USA even 80% of among all used antimicrobials have been used in food-producing animals [3, 20]. The European Medicines Agency (EMA) published the latest annual report on the sales of veterinary antibiotics according to the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project in October 2017. The newest report had shown that the sales of veterinary antimicrobial agents in 2015, also the sales of antibiotics for use in animals in Europe fell by 13.4% between 2011 and 2015. The sales of veterinary antimicrobial agents for food-producing animals (including horses), *expressed as mg sold per population correction unit (PCU)*, range from 2.9 mg/PCU to 432.2 mg/PCU in 30 European countries in 2015 [26]. According to Figure 1, the sales of tetracyclines, penicillins and sulfonamides accounted for 69.6 % of the total sales. Indeed, 0.1 % was considered for by first- and 2nd-generation cephalosporins, 0.2 % were for third- and 4th-generation cephalosporins, 1.2 % were for amphenicols, and 0.4 % for other quinolones. Many reports suggest that large rate of antibiotics used on animal husbandry. Moreover, for 2030 estimates, China and the USA will be at the top of the list of animal antibiotic consumption. One of the results linked the overuse of antibiotics is that 75-90% of antibiotics used in food-producing animals are excreted into the environment without metabolized [3]. Moreover, food-producing animals are an important reservoir of commensal or pathogenic (zoonotic) strains that have AMR genes [27, 28].These pathogens can spread by direct contact or indirectly through barn air, faecal material, water, soil, contaminated animal food and during slaughter to the environment or human [7, 20, 27]. Also, AMR bacteria can be transfer to the environment, other animal or calves with waste milk, colostrum, udder infections (mastitis) or medicines such as antibiotics. Another problem is the use of waste milk for calf feeding that is not suitable for human consumption. [29, 30]. The widespread, extensive and unappropriated use of antibiotic agents in the dairy farm has imposed selective pressure among pathogens and commensal bacteria in dairy cattle [31]. Also, researchers have expressed that potential sources of AMR genes are commensal bacteria from the intestinal of farm animals such as *Enterococcus* spp., *E. coli*. These bacteria can spread through direct contact or indirectly, through food, water, and animal waste application to farm fields. Also, these resistance genes can be transferred to zoonotic and other bacteria via bacterial mating (conjugation) through genetic elements such as plasmids, or by natural selection or genetic mutation, which is caused by environmental factors. [7, 32, 33, 34].

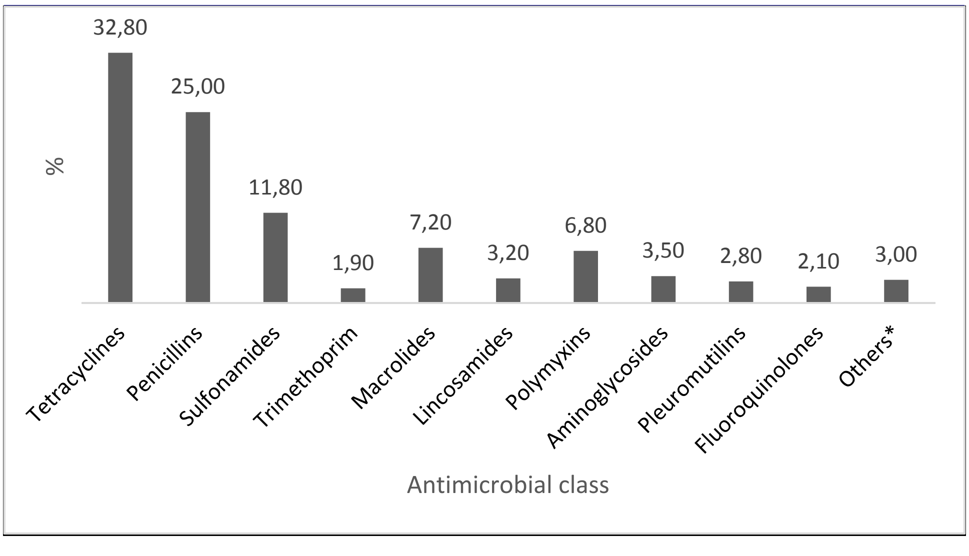

Fig. 1 Sales of antimicrobial agents by antimicrobial class as a percentage of the total sales for food-producing animals (in mg/PCU) aggregated by 30 European countries, for 2015 [26]. * Amphenicols, cephalosporins, other quinolones and other antibacterials.

4. Antibiotic-resistant bacteria in milk and dairy products

The extensive use of antibiotics in dairy farms causes the selection of multiple drug-resistant strains among the microbial species then these strains can be spread to milk and dairy products in many ways [31]. In recent years, many studies described emerging AMR bacteria in milk and dairy products. The over-use and misuse of the antimicrobials in the treatment of disease such as mastitis in dairy cattle led to the transfer of AMR bacteria to raw milk. Also, raw milk can be contaminated with AMR microorganisms through environmental factors such as barn condition, milking hygiene, farmer behaviour, and during raw milk transportation and storage. After raw milk collected by dairies, cross-contamination should be avoided by applying effective food safety and hygiene standards in dairy processing steps [35]. Figure 2 summarizes potential factors related to transmission of AMR bacteria or genes to raw milk and dairy product.

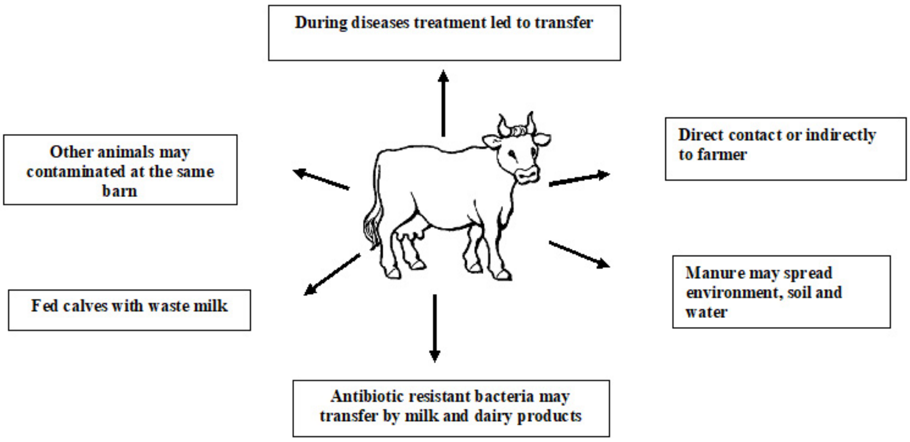

Fig. 2 Transmission ways of antibiotic-resistant bacteria from cattle.

In previous studies, various researchers have reported the presence of AMR bacteria in milk and dairy products. Table 3 shows a list of relevant research related to the isolation of antibiotic-resistant bacteria in milk and dairy products. For a long time, researchers' interest in the world has focused on the identification of antibiotic resistance genes in microorganisms isolated from mastitis milk, from food animal faecal swabs, and randomly collected food samples. Many researchers have determined AMR bacteria among particularly mastitis pathogens because mastitis is the main cause for the use of antimicrobial agents in dairy cattle [31]. Also, some of these studies have focused on raw milk with mastitis. A few studies reported about AMR of non-pathogenic raw milk-spoiling bacteria such as *Pseudomonas*, Enterobacteriaceae, and some psychrotrophs that make considerable problems in the quality of milk and dairy products [31]. Also, some researcher focused on AMR genes in starter culture bacteria lactobacillus [36]. Nowadays, the most of the studies focused on both pathogenic and nonpathogenic AMR bacteria, in milk and dairy product. Also, in the last decades, the antibiotics resistance has been well documented in the family of Enterobacteriaceae, especially *Klebsiella* spp., *Escherichia coli* (*E. coli*) followed by *Enterobacter*, *Enterococcus* in milk and dairy products,. Before of the ESBL producing bacteria, methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE) were investigated [38,39,40,41]. Many researchers highlighted that a potential risk of transferring ESBL (Extended-spectrum β-lactamase), AmpC (the aminopenicillin inactivating cephalosporinase), carbapenemase (CP) producing bacteria such as Enterobacteriaceae to consumer through the bulk tank milk [31, 42, 43, 44, 45]. Extended-spectrum β-lactamases (ESBL) are enzymes that can hydrolyze third-generation cephalosporins (oxyimino-cephalosporins), such as ceftriaxone, cefpirome, and cefepime. They are also partially susceptible to cephamycin and carbapenem. The ESBL are usually inhibited by β-lactamase inhibitors such as clavulanic acid, sulbactam, and tazobactam, furthermore, AmpC type beta-lactamases show resistance to cephalosporins in the 4th generation beta-lactam antibiotics and carbapenems [35]. AmpC is related to multiple antibiotic resistance and, the co-existence ESBL and AmpC β-lactamase caused limited treatment of infections in both humans and animals by pathogen [45, 46]. By also Tenhagen et al. and Virgin et al. have studied methicillin-resistant *Staphylococcus aureus* in the bulk milk tank [39, 41. As results of investigations, at least one bacteria whether it is a pathogen or not have AMR genes have been found. Even if this microorganism is not intrinsically AMR, they can achieve resistance genes through mobile genetic elements such as plasmids, transposons and bacteriophage. However, the patterns of resistance are very different due to resistance-encoding genetic elements can exchange easily to the same or different microorganisms.

Even though many governments have given legal permission for producers to sell raw milk and raw milk cheeses directly, these products, as a possible vehicle for AMR, create a potential risk for public health [45]. Several researchers investigated the occurrence of antibiotic-resistant bacteria in different kind of artisanal cheeses. The presence of ESBL, AmpC producing Enterobacteriaceae, *Enterococcus* spp. *E.coli*, *Enteropathogenic E. coli* (EPEC) and MRSA *Staphylococci* strains have been investigated on these cheeses. Also, researchers examined the susceptibility of isolates to some antimicrobial agents and had reported that isolates were more resistant to tetracycline, oxacillin, ampicillin and penicillin than other agents [38, 40, 47, 48, 49, 50, 51, 52, 53]. Milk and dairy product can be easily contaminated by microorganisms without hygienic condition and all of the bacteria may enter the mishandled milk and dairy process, and some of them cause foodborne outbreaks [54]. If these bacteria have AMR genes or acquire during the production such as handling, packing, transporting and marketing, this can lead to public health issues [45]. Regarding the final consumer, it is critical to analyze from random samples collected at the market. However, AMR bacteria or genes cannot originate from raw materials. Furthermore, the possibility of AMR bacteria or gene contamination/transmission is quite possible without raw material. Random sampling on the market will not be enough to prove that milk is the main reservoir of AMR bacteria or AMR genes. There are many production stages in the production of dairy products such as yoghurt, ice cream, butter and cream. Also, the environment and personnel can be an contamination source until consuming. Researchers should be followed the whole process most of the researchers studied with dairy products such as yoghurt, ice cream, butter and cream by random sampling [36, 37, 40, 55, 56, 57, 58]. Özdikemnli Tepeli and Zorba followed all of cheese production proses from milk to cheese; they analysed to find ESBL producing Enterobacteriaceae. Very few studies have been reported throughout food production (from farm to fork) [35].

5. Methods used in the determination of Antibiotic-resistant bacteria

In many studies, the antibiotic susceptibility was determined by disc diffusion method (DDM), microdilution assay (MIC), E-test, according to the Clinical and Laboratory Standards Institute (CLSI) and The European Committee on Antimicrobial Susceptibility Testing (EUCAST). CDC, WHO, EFSA and other society of government have issued recommendations for laboratory testing for AMR genes. Also, the double-disc combination method (DDCM), modified Hodge test (MHT), combination disc diffusion test (CDDT), double disc synergy test (DDST) have been used for phenotypic confirmation of some AMR. Further, some results that are positive as phenotypic have been confirmed by a molecular test that based on PCR and sequencing analysis for frequently detection AMR genes such as SHV, TEM, CTXM, SHV, and AmpC. While phenotypic screening tests to detect AMR are available, molecular tests are also expensive to most microbiological laboratories. Some researchers have pointed out that the AMR phenotypic screening test results may be misinterpreted if the bacteria carry AMR genotypes such as AmpC, ESBL and carbapenem together. Researchers are continuing to work on new, inexpensive and short-term diagnostic methods to detect AMR.

Table 3 Shows a list of relevant research related to the isolation of antibiotic-resistant bacteria in milk and dairy product.

Samples	Investigated antibiotic resistance	Used method	Investigated bacteria	Investigated genetic determinants	Detected widespread resistance	References
Milk, cheese	Extended-spectrum β-lactamase (ESBL), the aminopenicillin inactivating cephalosporinase (AmpC)	Disk diffusion method (DDM),	Enterobacteriaceae	-	AmpC *E.coli*	Tepeli and Zorba, 2018
Bulk milk tank	ESBL	The modified double disc combination method (DDCM)	O157, Non-O157 *E.coli*	-		Ntuli et al., 2017
Raw milk cheese, experimental raw milk fresh cheese, and pasteurised milk cheeses	β-lactams, macrolides, tetracyclines	Moleculer (M)	*Enterococcus faecalis* *Klebsiella pneumoniae* *Proteus. vulgaris*	tet(M), tet(L), erm(B), blaSHV, bla(Z)	erm(B), tet(M)	Bassi et al., 2016
Bulk milk tank	Susceptibility to some antimicrobial agents	DDM	Pseudomonas Enterobacteriaceae		Ampicillin	Decimo et al.,2016
Traditional cheese 'Sürk.'	Susceptibility to some antimicrobial agents, ESBL	DDM, M	*E.coli*	*bla*$_{TEM}$, *bla*$_{OXA}$, *bla*$_{SHV}$, and *bla*$_{CTX}$	Tetracycline, *bla*$_{CTX-M-15}$	Kürekci et al.,2016
Bulk milk tank	ESBL, AmpC, carbapenemase phenotypes	DDM, microdilution assay (MIC), M	Enterobacteriaceae	TEM, SHV and CTX-M	*bla*$_{CTX-M}$ group 1	Odenthal et al., 2016
Cheese	ESBL, AmpC	DDM, DDCM, and MIC	Enterobacteriaceae	-	ESBL *K. pneumoniae*	Özadam and Özpınar, 2016
Raw cow milk, and	ESBL, AmpC	DDM, MIC, and M	Enterobacteriaceae	*bla*$_{TEM}$, *bla*$_{SHV}$, and *bla*$_{CTX}$	*bla*$_{TEM}$	Tekiner and Özpınar,2016

raw cow milk cheese						
Milk, and cheese	Susceptibility to some antimicrobial agents, ESBL, the plasmid-mediated quinolone resistance genes (PMQR), the florfenicol resistance gene	DDM, and M	Shiga toxin-producing *Escherichia coli* (STEC) O157: H7	TEM, SHV, CTX-M, OXA, CMY, *qnr*A, *qnr*B, *qnr*S, *aac*(6′)-*Ib-cr*, and *flo*R	Kanamycin, *bla*$_{TEM-1,}$ *qnr*B, *flo*R	Ahmet and Shimamoto, 2015
Raw and pasteurised milk	Susceptibility to some antimicrobial agents, ESBL,	DDM, DDCM	*Proteus* spp.	-	Ampicillin	Fatah et al., 2015
Milk	Susceptibility to some antimicrobial agents, ESBL, AmpC, carbapenemase, Metallo-beta-lactamase	DDM, ESBL E-test, MIC, cefoxitin–cloxacillin double disc synergy (CC-DDS) test and AmpC beta-lactamase (ACBL), modified Hodge test (MHT) and, combination disc diffusion test (CDDT), and M	*E.coli*	*bla*$_{TEM}$, *bla*$_{SHV}$, *bla*$_{CTXM}$, *bla*$_{AmpC}$, *bla*$_{OXA,}$ *qnr*A, *qnr*B and *qnr*S, *sul1*	*bla*$_{SHV,}$ *bla*$_{TEM}$, *bla*$_{CTXM}$, *bla*$_{SHV}$, *bla*$_{ampC}$	Kar et al., 2015
Raw milk, cheese	Susceptibility to some antimicrobial agents	DDM	*E.coli*	-	Ampicillin	Kyere et al., 2015
Bulk tank milk from dairy farms	ESBL, AmpC, *K. pneumoniae* carbapenemase (KPC), metallo-b-lactamase (MBL)	DDCM, MIC, M	*K.pneumoniae*	*bla*$_{TEM}$, *bla*$_{SHV}$, and *bla*$_{CTXM}$	*bla*$_{SHV}$	Sudarwanto et al.,2015
Bryndza cheese	Susceptibility to some antimicrobial agents	DDM, M	*Enterococcus* spp. and *E.coli*	*bla*$_{TEM}$, *bla*$_{SHV}$, and *bla*$_{CTXM}$	Tetracycline, *bla*$_{TEM}$,*E.coli*	Vrabec et al., 2015
Milk, cheese	Susceptibility to some antimicrobial agents, ESBL	DDM, double-disc synergy test (DDST), M	*E.coli*	PER, VEB, TEM and CTX-M genes	Amoxicillin-clavulanic acid, CTX-M	Khoshbakht et al., 2014
Cheese, milk, butter, cheese spreads, yoghurt, cream, and butter	Susceptibility to some antimicrobial agents	DDM, M	*E.coli,K.pneumoniae, K. oxytoca,K.ornithynolitica, Serratia odorifera, E.aerogenes, Hafnia alvei*	blaCTX-M, blaTEM, tetA, tetB, tetC and tetD	Ampicillin,	Mateescu et al., 2014
Bulk tank milk	Methicillin-resistance	MIC, M	*Staphylococcus aureus*	spa types, t011, t034,t1457,	t011, t034	Tenhagen et al., 2014
Raw milk, cheeses, yoghurts, and butter	Vancomycin-resistant	DDM, MIC,	Vancomycin-resistant enterococci (VRE)	-	None	Çetinkaya et al., 2013
Raw milk, white cheese and ice cream	Susceptibility to some antimicrobial agents, ESBL	DDST	*Klebsiella* spp.		Ampicillin	Gundogan and Avci, 2013
Minas soft cheese	Susceptibility to some antimicrobial agents	VITEK, MIC	Enteropathogenic *E. coli* (EPEC)	-	Ampicillin	Dias et al., 2012
Bulk milk tank, mastitis milk	Susceptibility to some antimicrobial agents, ESBL	DDM, E-test, ESBL strip, M	Enterobacteriaceae	*bla*$_{TEM}$, *bla*$_{SHV}$, and *bla*$_{CTXM}$	*bla*$_{CTXM}$, *bla*$_{TEM}$,	Geser et al., 2012
Cream cheeses, soft cheeses, semi-hard cheeses, hard- and processed cheeses, produced from pasteurized milk and soft cheeses, semi-	Methicillin-Resistant	Brilliance MRSA 2 agar and M	*Staphylococcus aureus*	*mecA*		Zinke et al., 2012

hard- and hard cheeses, made from raw milk						
Cheese	Susceptibility to some antimicrobial agents	DDM, E- test	*E. coli, Staphylococci*	-	Tetracycline, oxacillin	Saleh et al., 2011
Raw milk, commercial and traditional cheese, ice cream, yoghurt, dough, butter, kashk	Susceptibility to some antimicrobial agents	DDM	*Listeria* spp.	-	Nalidixic acid	Rahimi et al., 2010
Portuguese cheese	Susceptibility to some antimicrobial agents, ESBL	DDM, DDCM	Enterobacteriaceae	bla_{TEM}, bla_{SHV}, and bla_{CTXM}	bla_{TEM}	Amador et al., 2009
Baladi cheese, Shankleesh, and Kishk	Susceptibility to some antimicrobial agents	DDM	*L.monocytogenes*	-	oxacillin	Harakeh et al., 2009
Bulk tank milk	Methicillin-resistant	Genotypic and phenotypic methods	*S.aureus*	nuc and mecA,		Virgin et l., 2009
White cheese homemade	Susceptibility to some antimicrobial agents	DDM	*Listeria* spp	-	Penicillin	Arslan and Özdemir, 2008
Milk, natural starter cultures and cheeses	Vancomycin	DDM	*E. faecalis and E. faecium*	vanA and vanB		Cariolato et al., 2008
Raw milk, pasteurized milk, ice cream, white cheese	ESBL	DDM, DDST	*Klebsiella* spp.		Ampicillin, amoxicillin	Gundogan and Yakar, 2006
Raw milk cream, yoghurt, hand-made cheese, and industrially produced white cheese samples	Susceptibility to some antimicrobial agents	M	Lactobacilli	tet(M), cat-TC, erm(ABC), and van(A)	None	Çataloluk and Gogebaakn, 2004

DDM: Disk diffusion method, DDCM: double disc combination method, M: Molecular, MIC: microdilution assay, CC-DDS: cefoxitin-cloxacillin double disc synergy test,ACBL: AmpC beta-lactamase, MHT: modified Hodge test, CDDT: combination disc diffusion test, DDST: double-disc synergy test,

6. Conclusions

Several studies on human, food-animals, and food revealed that some antibiotic-resistant strains are the same. However, the effect of the antibiotic-resistant bacteria observed in food to the human health is still uncertain [46]. The results obtained in the recent studies revealed that the use of antibiotics could not be controlled effectively in a dairy farm, also disregarding potential risk to human health from food-producing the animal. Food- producing animals are one of the primary transmitters of antibiotic-resistant bacteria to humans and one of the most incriminated foods about antibiotic resistant bacteria and antibiotic resistance genes is milk and dairy products [45]. Further research is needed throughout the food chain to suggest that milk and dairy products are main reservoirs of AMR bacteria. Also, raw milk and some dairy products carry a potential risk for human health regarding AMR bacteria Milking hygiene, raw milk chain, food production process, end product transporting and storage conditions are the more important for transmission of AMR bacteria. Furthermore, consumption and preservation method such as cooking time and temperature at home is not to be ignored. Effective risk assessment, appropriate food safety targets and adequate prevention strategies should be developed to remove AMR bacteria from the market. This study emphasizes that milk and dairy products have a potential risk for human health for AMR today.

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