Review article

Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae in cattle production – a threat around the world

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ARTICLE INFO

Keywords: Microbiology Food microbiology Cattle Antibiotic resistance Antibiotic resistant bacteria

ABSTRACT

Food producing animal is a global challenge in terms of antimicrobial resistance spread. Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae are relevant opportunistic pathogens that may spread in many ecological niches of the One Health approach as human, animal and environment due to intestinal selection of antimicrobial resistant commensals in food production animals. Cattle production is a relevant ecological niche for selection of commensal bacteria with antimicrobial resistance from microbiota. Enterobacteriaceae show importance in terms of circulation of resistant bacteria and antimicrobial resistance genes via food chain creating a resistance reservoir, setting up a threat for colonization of humans and consequent health risk. ESBL-producing Enterobacteriaceae are a threat in terms of human health responsible for life threatening outbreaks and silent enteric colonization of community populations namely the elder population. Food associated colonization is a difficult to handle and control. In a time of globalization of food trading, population intestinal colonization is a mirror of food production and in that sense this work aims to make a picture of ESBL-producing Enterobacteriaceae in animal production for food over the world in order to make some light in this reality of selection of resistant threats in food producing animal.

1. Introduction

Extended-spectrum beta-lactamas (ESBL) are enzymes responsible for the hydrolysis of oxyimino-beta-lactam antibiotics, which are important therapeutic agents for the treatment of serious human and animal infections. ESBL were first described in 1983 in Enterobacteriaceae (new taxonomy Enterobacterales) and since then, with the research of the scientific community, it has been observed that ESBL-producing Enterobacteriaceae (E-ESBL) are a real threat to human health, being responsible for 1700 deaths in the USA due to therapeutic failure in severe infections in 2013 (Adeolu et al., 2016; CDC, 2013; Knothe et al., 1983). However, E-ESBL are not only limited to hospital environment, they are also present as human intestinal commensals (Gonçalves et al., 2016; Karanika et al., 2016). The presence of E-ESBL in several ecological niches, as commensals in humans and animals and as environmental contaminants, is reported worldwide, however, in the last decades a niche that has raised great concern, for being able to function as a reservoir and vehicle of transmission and dissemination of E-ESBL is the production animals due to their direct connection with the food chain (Madec et al., 2017).

Cattle are one of the main sources of animal protein, becoming one of the most consumed meat around the world and milk, one of the main constituents of the human food chain (Alexandratos and Bruinsma, 2012). It is also one of the main sources of biological fertilizers, due to the high production of faecal mass of these animals (Smith and Williams, 2016). All this, highlights the importance of cattle production in the context of the food chain and the contaminated environment as reservoir and transmitting/disseminating vehicle of E-ESBL, thus configuring a threat to the world public health. This circulation of E-ESBL within our ecosystem creates a consensual concern of the scientific community and of the authority involved in the One health approach (Robinson et al., 2016).

The ESBL are enzymes that are classified in several types, being CTX-M, SHV and TEM the most prevalent around the world (Paterson and Bonomo, 2005). However, there are other ESBL such as OXA, PER, VEB, BES, GES, SFO, TLA, and IBC (Paterson and Bonomo, 2005). The CTX-M
are enzymes with environmental origins which are currently the most widespread type of ESBL and are commonly associated with E-ESBL reports (Cantón et al., 2012). Variants such as CTX-M-15, responsible for infectious outbreaks around the world, are associated with a clone responsible for extraintestinal *E. coli* infections resistant to antibiotics, the ST131 (Price et al., 2013).

The objective of this study was to make an insight about the epidemiology of the spread of E-ESBL and the ESBL genes distribution in cattle around the world, in order to update the current scenario of E-ESBL dissemination through cattle production in all continents.

2. ESBL producing *Enterobacteriaceae* in cattle - a global view

The first description of an E-ESBL in cattle was in Japan, where a CTX-M-2 *E. coli* producer was detected in cattle faeces from an important region close to the centre of the country (Shiraki et al., 2004). From the first description to the present, E-ESBL has already been described in cattle production in 39 countries, with more concentration in Europe (n = 16) and Asia (n = 13) as shown in Figure 1. The origins of E-ESBL are diverse, being isolated from healthy animals (faecal samples) or from veterinary clinical origin (mastitis, diarrheal processes, infections or with any other pathological picture). The countries with the highest reports on E-ESBL in cattle, are the United Kingdom (n = 14), Germany (n = 11), France (n = 9) and the United States (n = 9), the last one being the world’s largest cattle producer, and the 3 Europeans, 4th, 3rd and 1st, respectively, in number of cattle in Europe (Eurostat, 2016; USDA et al., 2017). Within the 5 world largest cattle producers (United States, Brazil, the European Union, China and India) there have been reports of animals harbouring commensal or clinical E-ESBL. The Table 1 shows all the descriptions of E-ESBL in cattle around the World, including the source, species and ESBL gene.

The most frequent ESBL types in E-ESBL in cattle, as expected, were the ones of CTX-M-1 group with higher prevalence for CTX-M-1, CTX-M-14 and CTX-M-15. CTX-M-1 was reported in 20 countries, most frequently in Europe (n = 14), being found in Germany, Denmark, Spain, Finland, France, Hungary, Portugal, Netherlands, United Kingdom, Czech Republic, Slovakia, Sweden, Switzerland and Turkey. CTX-M-1 was first described in human E-ESBL in 1989 in Germany, and it has also been reported in other European countries such as Spain, France, Italy and United Kingdom as well as in Asia and North America (Cantón and Coque, 2006; Moosavian and Ahmadkhojastehsvay, 2016; Wang et al., 2013).

CTX-M-15 and CTX-M-14 are the most important CTX-M enzymes due to their large diffusion and relation to outbreaks and severe extraintestinal infections (Cantón et al., 2012; Matsumura et al., 2015; Price et al., 2013). CTX-M-14 was described in E-ESBL in cattle in 13 countries, mainly in Europe (Germany, Belgium, France, Netherlands, United Kingdom, and Switzerland) and in Asia (China, South Korea, Hong Kong, Japan, and Taiwan), as well as the United States and Oceania. CTX-M-15 was first described in 2002 in E-ESBL from a hospital in China (Chana-wong et al., 2002; Ma et al., 2002). E-ESBL producers isolated from human of CTX-M-14 type are described in Europe, Asia, North and South America, Africa and Oceania, many times related to pandemic clones such as *E. coli* ST131 responsible for outbreaks in the last years (Cantón et al., 2008; Chen et al., 2014; Giedraitiene et al., 2017; Peirano et al., 2010, 2011; Pitout et al., 2005; Shin et al., 2011; Silva and Lincopan, 2012; Zong et al., 2009).

CTX-M-15 was first described in 2001 in E-ESBL isolate in a hospital in New Delhi, India, and today is the most widespread ESBL in the various niches and the most important of all, due to its high relation to important, for human health, E-ESBL clones (Cantón et al., 2012; Clermont et al., 2008; Karim et al., 2001; Kim et al., 2017; Price et al., 2013; Woodford et al., 2004). E-ESBL producing CTX-M-15 in cattle were described in 21 countries around the world, present in most of Europe, being reported in Germany, France, Italy, Netherlands, United Kingdom, Sweden, Switzerland and Turkey. In Asia they were described in China, South Korea, India, Israel, Japan, Lebanon and Taiwan and also reported in North and South America (Brazil, Canada and United States) and Africa (Egypt, Tanzania and Tunisia).

CTX-M-15 has been reported in all continents (Europe, North America, South America, Asia, Africa, Oceania and Antarctica with reports in all major ecological niches (humans, animals, and environment), these E-ESBL producers of CTX-M-15 are an excellent example of the public health threat that involves circulation of resistant Enterobacteriaceae and resistance genes among the different ecological niches that is currently evidenced under the prism of the “One Health” approach (Chen et al.,

Figure 1. World map illustrating the countries with description of E-ESBL in cattle.
| Beta-lactamase | Enterobacteriaceae | Country       | Source                        | Reference                          |
|----------------|--------------------|---------------|-------------------------------|------------------------------------|
| **CTX-M-1**    | *Escherichia coli* | Europe        | Faecal                        | (Wieler et al., 2011)              |
|                |                    | Germany       | Mastitis                      | (Freitag et al., 2017; Michael et al., 2017) |
|                |                    |               | Diarrheic                     | (Swers et al., 2014)               |
|                |                    |               | Sick                          | (Michael et al., 2017)             |
|                |                    |               | Infection                     | (Brennan et al., 2016)             |
|                |                    | Denmark       | Commensal                     | (Kjeldsen et al., 2015)            |
|                |                    |               | ND                            | (Garcia-Fernandez et al., 2011; Jakobsen et al., 2015) |
|                |                    | Spain         | Mastitis                      | (Britias et al., 2005)             |
|                |                    | Finland       | Faecal                        | (Pälvarinta et al., 2016)          |
|                |                    | France        | Faecal                        | (Haenni et al., 2014; Hartmann et al., 2012; Madec et al., 2008; Meunier et al., 2006) |
|                |                    |               | Mastitis                      | (Dahmen et al., 2013)              |
|                |                    |               | Diarrheic                     | (Hartmann et al., 2012)            |
|                |                    |               | Sick                          | (Madec et al., 2006; Valat et al., 2016) |
|                |                    |               | Infection                     | (Meunier et al., 2006)             |
|                |                    | Hungary       | Infection                     | (Toth et al., 2013)               |
|                |                    | Portugal      | Faecal                        | (Ramos et al., 2013)              |
|                |                    | Mayotte       | ND                            | (Gay et al., 2018)                |
|                |                    | Netherlands   | Faecal                        | (Cecarelli et al., 2019; Heuvelink et al., 2019; Hoerdijk et al., 2013a, b, c) |
|                |                    | United Kingdom| Faecal                        | (Velasova et al., 2019)           |
|                |                    |               | Infection                     | (Hunter et al., 2010)             |
|                |                    |               | ND                            | (Stokes, 2014)                    |
|                |                    | Czech Republic| Faecal                        | (Dolejska et al., 2011b)          |
|                |                    |               | Sick                          | (Dolejska et al., 2013)            |
|                |                    | Réunion       | ND                            | (Gay et al., 2018)                |
|                |                    | Slovakia      | Faecal                        | (Kmei and Bujňáková, 2018)        |
|                |                    | Sweden        | Faecal                        | (Dane et al., 2019)               |
|                |                    | Switzerland   | Faecal                        | (Indimiani et al., 2012; Genser et al., 2012a; Zurfsh et al., 2015) |
|                |                    | Turkey        | Faecal                        | (Atalantaş et al., 2017; Pehlivanoglu et al., 2016) |
|                |                    | North America | Canada                        | (Cormier et al., 2019)            |
|                |                    |               | USA                           | (Mir et al., 2016; Mollenkopf et al., 2012; Wittum et al., 2010) |
|                |                    | Asia          | China                         | (Ali et al., 2016, 2017)           |
|                |                    |               | South Korea                   | (Park et al., 2017)               |
|                |                    |               | Indonesia                     | (Sudarwanto et al., 2016)         |
|                |                    | Japan         | Mastitis                      | (Ohnishi et al., 2013b)           |
|                | **Klebsiella pneumoniae** |        | Europe                        |                                   |
|                |                    | Italy         | Mastitis                      | (Locatelli et al., 2010)          |
|                | **Klebsiella oxytoca** | Italy        | Faecal                        | (Stefani et al., 2014)            |
|                | **Salmonella enterica** | Germany     | ND                            | (Rodríguez et al., 2009)          |
| **CTX-M-1/61** | *E. coli*          | Europe        | Faecal                        | (Dahms et al., 2015)              |
|                |                    | Germany       |                               |                                    |
| **CTX-M-2**    | *E. coli*          | South America | Brazil                        | (Palmeira et al., 2018)           |
|                |                    | Europe        |                               |                                    |
|                |                    | Germany       | Mastitis                      | (Eisenberger et al., 2017; Freitag et al., 2017; Michael et al., 2017) |
|                |                    |               | Sick                          | (Michael et al., 2017)            |
|                |                    | Netherlands   | Faecal                        | (Cecarelli et al., 2019; Heuvelink et al., 2019) |
|                |                    | North America | Canada                        | (Cormier et al., 2016)            |
|                |                    | Asia          | Japan                         | (Shiraki et al., 2004)            |
|                |                    |               | Diarrheic                     | (Ohnishi et al., 2013a)           |
|                |                    |               | Infection                     | (Asai et al., 2011)               |
|                | **K. pneumoniae**  | Japan         | Mastitis                      | (Ohnishi et al., 2013a, b; Saishu et al., 2018) |
|                | **Klebsiella oxytoca** | Japan     | Mastitis                      | (Ohnishi et al., 2013b)           |
|                | **Citrobacter freundii** | Japan     | Mastitis                      | (Ohnishi et al., 2013a)           |
| Beta-lactamase | Enterobacteriaceae | Country | Source | Reference |
|----------------|--------------------|---------|--------|-----------|
| CTX-M-2/97     | *Citrobacter koseri* | Japan   | Mastitis | (Ohnishi et al., 2013b) |
|                | *Enterobacter cloacae* | Japan   | Mastitis | (Ohnishi et al., 2013a) |
|                | *Enterobacter aerogenes* | Japan   | Mastitis | (Ohnishi et al., 2013b) |
| CTX-M-3        | *E. coli*            | Europe  | Faecal  | (Hordijk et al., 2013a, b, c) |
| CTX-M-8        | *E. coli*            | Europe  | Faecal  | (Ceccarelli et al., 2019) |
| CTX-M-9        | *E. coli*            | Europe  | Faecal  | (Ceccarelli et al., 2019) |
|                | *S. enteric*         | Australia | ND   | (Sparham et al., 2017) |
| CTX-M-14       | *E. coli*            | Europe  | Faecal  | (Ceccarelli et al., 2019) |
|                |                     |         |        | (Heuvelink et al., 2019) |
|                |                     |         |        | (Hordijk et al., 2013a, b, c) |

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| Beta-lactamase | Enterobacteriaceae | Country | Source | Reference |
|---------------|-------------------|---------|--------|-----------|
| **K. pneumoniae** | Australia | Sick | (Abraham et al., 2015) |
|                | Europe | | | |
|                | France | Mastitis | (Dahmen et al., 2013) |
|                | Asia | | | |
|                | Japan | Mastitis | (Ohnishi et al., 2013b) |
| **CTX-M-15** | E. coli | South America | Brazil | Faecal | (Sartori et al., 2017) |
|                 | Europe | | | |
|                 | Germany | Faecal | (Fischer et al., 2014; Wieler et al., 2011) |
|                 | Mastitis | (Eisenberger et al., 2017; Freitag et al., 2017; Michael et al., 2017) |
|                 | Sick | (Michael et al., 2017) |
|                 | France | Faecal | (Haenni et al., 2014) |
|                 | Sick | (Madec et al., 2008) |
|                 | Infection | (Madec et al., 2012; Meunier et al., 2006) |
|                 | Madagascar | ND | (Gay et al., 2018) |
|                 | Mayotte | ND | (Gay et al., 2018) |
|                 | Netherlands | Faecal | (Cecarelli et al., 2019; Heuvelink et al., 2019; Hoedijk et al., 2013a, b, c) |
|                 | United Kingdom | Faecal | (Horton et al., 2011; Randall et al., 2014; Watson et al., 2012) |
|                 | Mastitis | (Timofte et al., 2014) |
|                 | Infection | (Hunter et al., 2010) |
|                 | Sweden | Faecal | (Duse et al., 2015) |
|                 | Switzerland | Faecal | (Endimiani et al., 2012; Genser et al., 2012a; Zurfluh et al., 2015) |
|                 | Turkey | Faecal | (Adalatça et al., 2017; Pehlivanoglu et al., 2016) |
| **Asia** | China | Faecal | (Zheng et al., 2019) |
|                 | Mastitis | (Ali et al., 2016, 2017) |
|                 | Israel | ND | (Lifshitz et al., 2018) |
|                 | South Korea | Faecal | (Tamang et al., 2013a) |
|                 | Mastitis | (Tark et al., 2017) |
|                 | Japan | Faecal | (Unu et al., 2013) |
|                 | Mastitis | (Ohnishi et al., 2013b) |
|                 | Diarrheic | (Ohnishi et al., 2013a) |
|                 | Lebanon | Faecal | (Diab et al., 2016) |
|                 | Taiwan | Mastitis | (Su et al., 2016) |
| **North America** | Canada | ND | (Cormier et al., 2019) |
|                 | Faecal | (Cormier et al., 2016) |
|                 | USA | Faecal | (Mir et al., 2016; Mollenkopf et al., 2012) |
| **Africa** | Egypt | Faecal | (Braun et al., 2016) |
|                 | Tanzania | Faecal | (Seni et al., 2016) |
|                 | Tunisia | Faecal | (Graimi et al., 2014) |
|                 | Mastitis | (Saidani et al., 2018) |
| **K. oxytoca** | Europe | | | |
|                | France | Faecal | (Haenni et al., 2014) |
|                | Asia | | | |
|                | India | Mastitis | (Kovapra et al., 2016) |
| **K. ozaenae** | Europe | | | |
|                | Italy | Faecal | (Stefani et al., 2014) |
| **K. oxytoca** | Asia | | | |
|                | Egypt | Mastitis | (Ahmed and Shimamoto, 2011) |
| **CTX-M-15/28** | E. coli | Europe | | | |
| **CTX-M-17** | E. coli | Asia | China | Faecal | (Zheng et al., 2019) |
| **CTX-M-17/18** | E. coli | Europe | United Kingdom | Faecal | (Liebana et al., 2006) |

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| Beta-lactamase | Enterobacteriaceae | Country       | Source          | Reference                          |
|---------------|--------------------|---------------|-----------------|------------------------------------|
| CTX-M-20      | E. coli            | Europe        | Infection       | (Hunter et al., 2010)              |
|               |                    | United Kingdom |                 |                                    |
| CTX-M-22      | E. coli            | Europe        | Faecal          | (Heuvelink et al., 2019)            |
| CTX-M-24      | E. coli            | North America | Faecal          | (Cormier et al., 2016)             |
|               |                    | Canada         |                 |                                    |
| CTX-M-27      | E. coli            | Europe        | Faecal          | (Ceccarelli et al., 2019)          |
|               |                    | Netherlands    |                 |                                    |
|               |                    | USA            | Faecal          | (Tadesse et al., 2018)             |
|               |                    | ND             |                 | (Afema et al., 2018)               |
|               |                    | Canada         | Faecal          | (Cormier et al., 2016)             |
|               |                    |               | ND              | (Cormier et al., 2019)             |
| CTX-M-28      | E. coli            | Asia          | Faecal          | (Ho et al., 2011)                  |
| CTX-M-32      | E. coli            | Europe        | Faecal          | (Haenni et al., 2014)              |
|               |                    | France         |                 |                                    |
|               |                    | Germany        | Mastitis        | (Eisenberger et al., 2017)         |
|               |                    | Mayotte        | ND              | (Gay et al., 2018)                 |
|               |                    | Netherlands    | Faecal          | (Ceccarelli et al., 2019; Heuvelink et al., 2019; Hordijk et al., 2013a, b, c) |
|               |                    | Portugal       | Faecal          | (Ramos et al., 2013)               |
|               |                    | United Kingdom | Infection       | (Hunter et al., 2010)              |
|               |                    | North America  |                 |                                    |
|               |                    | Canada         | Faecal          | (Cormier et al., 2016)             |
|               |                    | ND             |                 | (Cormier et al., 2019)             |
|               |                    | USA            | Faecal          | (Cottell et al., 2013; Poole et al., 2017) |
|               |                    | Asia           | Faecal          | (Tamang et al., 2013a)             |
| CTX-M-55      | E. coli            | Europe        | Sick            | (Haenni et al., 2018; Lupo et al., 2018) |
|               |                    | France         | Faecal          | (Ceccarelli et al., 2019; Heuvelink et al., 2019) |
|               |                    | Spain          | Faecal          | (Hernández et al., 2017)           |
|               |                    | North America  | Faecal          |                                    |
|               |                    | Canada         | Faecal          | (Cormier et al., 2016)             |
|               |                    | ND             |                 | (Cormier et al., 2019)             |
|               |                    | Asia           | Faecal          | (Tamang et al., 2013a)             |
|               |                    | China          | Faecal          | (Zheng et al., 2012, 2019)         |
|               |                    | Mastitis       | (Ali et al., 2016, 2017) |
|               |                    | Hong Kong      | Faecal          | (Ho et al., 2011, 2013)            |
|               |                    | Taiwan         | Mastitis        | (Su et al., 2016)                  |
| CTX-M-57      | E. coli            | Europe        | Faecal          | (Haenni et al., 2014)              |
| CTX-M-61      | E. coli            | North America  | Faecal          | (Cormier et al., 2016)             |
| CTX-M-63      | K. pneumoniae      | Asia          | Faecal          | (Koovapra et al., 2016)            |
|               |                    | India          | Mastitis        |                                    |
| CTX-M-65      | E. coli            | Europe        | Faecal          | (Ceccarelli et al., 2019; Heuvelink et al., 2019) |
|               |                    | Netherlands    | Faecal          | (Cormier et al., 2016)             |
|               |                    | North America  | Faecal          |                                    |
|               |                    | Canada         | Faecal          | (Cormier et al., 2016)             |
|               |                    | ND             |                 | (Cormier et al., 2019)             |
|               |                    | S. enterica    | ND              | (Tate et al., 2017)                |
| CTX-M-79      | E. coli            | Europe        | Faecal          | (Hordijk et al., 2013c)            |
|               |                    | Netherlands    | Faecal          | (Hordijk et al., 2013c)            |
|               |                    | North America  | Faecal          | (Wittum et al., 2010)              |
|               |                    | USA            | Faecal          | (Wittum et al., 2010)              |
| CTX-M-98      | E. coli            | Asia          | Faecal          | (Ho et al., 2011)                  |

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| Beta-lactamase                        | Enterobacteriaceae | Country         | Source   | Reference                        |
|--------------------------------------|--------------------|-----------------|----------|----------------------------------|
| **CTX-M-115**                        | *E. coli*          | North America   | Faecal   | Cormier et al., 2016            |
| **CTX-M-117**                        | *E. coli*          | Europe          | Faecal   | (Hächler et al., 2013; Zurfluh et al., 2015) |
| **CTX-M-123**                        | *E. coli*          | Asia            | Faecal   | Ho et al., 2015                  |
| **CTX-M-132**                        | *E. coli*          | Asia            | Faecal   | Ho et al., 2015                  |
| **CTX-M-172**                        | *E. coli*          | North America   | Faecal   | Cormier et al., 2016            |
| **CTX-M – without variant description** | *E. coli* | Europe          | Faecal   | Wu et al., 2013                  |
|                                      |                    | France          | Diarrheic | Valat et al., 2012              |
|                                      |                    | Netherlands     | Faecal   | Wu et al., 2013                  |
|                                      |                    | United Kingdom  | Faecal   | Wu et al., 2013                  |
|                                      |                    | Switzerland     | Faecal   | Geser et al., 2011              |
|                                      |                    | North America   | Faecal   | Awosile et al., 2018            |
|                                      |                    | USA             | Faecal   | Davis et al., 2015              |
|                                      |                    | Asia            | Faecal   | Yang et al., 2016               |
|                                      |                    | Saudi Arabia    | ND       | Hassan et al., 2015             |
|                                      | **K. pneumoniae**  | South America   | Mastitis | Nobrega et al., 2013            |
|                                      |                    | Asia            | Mastitis | Das et al., 2017                |
|                                      | **Salmonella sp**  | North America   | Sick     | Frye and Fedorka-Cray, 2007     |
| **SHV-2**                            | *E. coli*          | North America   | Faecal   | Cormier et al., 2016            |
| **SHV-5**                            | *E. coli*          | Europe          | Faecal   | Kurukbasmacı et al., 2008       |
|                                      |                    | Turkey          | Faecal   | Kurukbasmacı et al., 2008       |
|                                      | **C. freundii**    | Turkey          | Faecal   | Kurukbasmacı et al., 2008       |
|                                      | **C. brakii**      | Turkey          | Faecal   | Kurukbasmacı et al., 2008       |
| **SHV-11**                           | *E. coli*          | Asia            | Diarrheic | Ohnishi et al., 2013a           |
|                                      | **K. pneumoniae**  | Japan           | Diarrheic | Ohnishi et al., 2013a           |
| **SHV-12**                           | *E. coli*          | Europe          | Sick     | Michael et al., 2017            |
|                                      |                    | Germany         | Faecal   | Haenni et al., 2014; Madec et al., 2008 |
|                                      |                    | France          | Faecal   | Haenni et al., 2014; Madec et al., 2008 |
|                                      |                    | Netherlands     | Faecal   | Cecarelli et al., 2019; Hordijk et al., 2013c |
|                                      |                    | Turkey          | Faecal   | Kurukbasmacı et al., 2008; Pehlivanoglu et al., 2016 |
|                                      | **K. pneumoniae**  | Asia            | Mastitis | Ali et al., 2016, 2017          |
|                                      |                    | Egypt           | Mastitis | Ahmed and Shimamoto, 2011       |

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| Beta-lactamase | Enterobacteriaceae | Country | Source | Reference |
|---------------|-------------------|---------|--------|-----------|
| K. oxytoca    | Egypt Mastitis    | Ahmed and Shimamoto, 2011 |
| E. cloacae    | Egypt Mastitis    | Ahmed and Shimamoto, 2011 |
| SHV-28        | Serratia marcescens | Egypt Mastitis | Ahmed and Shimamoto, 2011 |
| K. pneumoniae | Asia              | India Mastitis | Koovapra et al., 2016 |
| SHV – without variant description | E. coli | Europe | Faecal | (Wu et al., 2015) |
|               | Asia Faecal       | (Borah et al., 2014) |
|               |Israel Faecal     | (Kar et al., 2015) |
|               | K. pneumoniae | South America | Mastitis | Nobrega et al., 2013 |
| Salmonella spp. | North America | USA Sick | Frye and Fedorka-Cray, 2007 |
| TEM-20        | E. coli | Europe | Faecal | (Hordijk et al., 2013c) |
| TEM-24        | K. ozaenae       | Europe | Faecal | Stefani et al., 2014 |
| TEM-52        | E. coli | Europe | Faecal | (Wiener et al., 2011) |
|               | Germany Faecal    | Michael et al., 2017 |
|               | France Diarrheic | Haenni et al., 2012 |
|               | Netherlands Faecal | Cecarelli et al., 2019; Heuvelink et al., 2018; Hordijk et al., 2013a, b, c |
| TEM-71        | E. coli | Europe | Faecal | Hartmann et al., 2012 |
|               | France Diarrheic | Hartmann et al., 2012 |
| TEM-126       | E. coli | Europe | Faecal | Madec et al., 2008 |
| TEM-186       | E. coli | Europe | Faecal | Geser et al., 2012a |
| TEM-190       | E. coli | Europe | Faecal | Cecarelli et al., 2019 |
| TEM – without variant description | E. coli | North America | USA Faecal | Donaldson et al., 2006; Mir et al., 2016 |
|               | Asia | (Borah et al., 2014) |
|               | Thailand Mastitis | Hinthong et al., 2017 |
|               | Africa | Egypt Faecal | Braun et al., 2016 |
| OXA-10        | E. coli | Europe | Faecal | Kurkbasnaci et al., 2008 |
|               | C. freundii      | Kurkbasnaci et al., 2008 |
|               | C. braakii       | Kurkbasnaci et al., 2008 |
| OXA-30        | K. oxytoca       | Africa | Mastitis | Ahmed and Shimamoto, 2011 |
|               | Egypt Mastitis   | Ahmed and Shimamoto, 2011 |
| ESBL producers - without beta-lactamase description (ND-ESBL) | E. coli | South America | Brazil Mastitis | Santos, 2006 |
|               | Chile Mastitis   | Gonzalez, 2006 |
|               | Peru Faecal      | Mendoza, 2017 |
|               | Europe | Germany Faecal | Friese et al., 2013 |
|               | Spain Faecal     | Britas et al., 2005 |
|               | Países de Gales | ND | Teale et al., 2005 |
|               | Netherlands Faecal | Goeppgrijp et al., 2016 |
|               | Switzerland Faecal | Reint et al., 2013 |
|               | North America    | |

(continued on next page)
### Table 1 (continued)

| Beta-lactamase          | Enterobacteriaceae | Country | Source       | Reference                  |
|-------------------------|--------------------|---------|--------------|----------------------------|
| Canada                  | Faecal             |         | Lussier, 2010|                            |
| Asia                    |                    |         |              |                            |
| Iran                    | Faecal             | Barzan et al., 2017 |                |
| Thailand                | Mastitis           | Hinthong et al., 2017 |          |
| Africa                  |                    |         |              |                            |
| Nigeria                 | Faecal             | Ogefere et al., 2017 |                |
| Tanzania                | Faecal             | Mkala and Azizi, 2017 |          |
| E. pneumoniae           | Asia               |         |              |                            |
| Israel                  | Faecal             | Adler et al., 2015 |                |
| Klebsiella spp.         | Africa             |         |              |                            |
| Nigeria                 | Faecal             | Ogefere et al., 2017 |                |
| Salmonella spp.         | Nigeria            | Ogefere et al., 2017 |                |
| C. youngae              | Europe             |         |              |                            |
| Switzerland             | Faecal             | Reist et al., 2013 |                |
| E. cloacae              | South America      |         |              |                            |
| Peru                    | Faecal             | Mendoza, 2017 |                |
| Europe                  |                    |         |              |                            |
| Switzerland             | Faecal             | Reist et al., 2013 |                |
| Proteus mirabilis       | Africa             |         |              |                            |
| Nigeria                 | Faecal             | Ogefere et al., 2017 |                |
| Proteus vulgaris        | Nigeria            | Ogefere et al., 2017 |                |
| Providencia spp.        | Nigeria            | Ogefere et al., 2017 |                |
| Shigella spp.           | Nigeria            | Ogefere et al., 2017 |                |

Source: ND – Not described isolate source.

**Figure 2.** Illustrative map of Europe showing countries with description of E-ESBL in cattle and beta-lactamas type.
2014; Dia et al., 2016; Fam et al., 2011; Hasan et al., 2016; Hernández et al., 2012; Liao et al., 2017; Poirel et al., 2013; Ruiz et al., 2011; Sidjabat et al., 2010).

The virulent and multi-resistant CTX-M-15-producing E. coli O25b-ST131 clone is certainly one of the most well adapted circulant clones among E-ESBL, which is responsible for outbreaks and deaths around the world and is not related only to infectious processes, but is also reported in human intestinal colonization (elderly, adults and children) and animals (terrestrial and aquatic) and environmental contamination (Badran et al., 2016; Brahmi et al., 2015; Dolejska et al., 2011a; Ewers et al., 2010; Gonçalves et al., 2016; Namaei et al., 2017; Naseer et al., 2007; Olesen et al., 2013; Oteo et al., 2009; Owens et al., 2011; Zhong et al., 2015).

3. Europe

Europe is the continent with more number of countries (n = 16) with description of E-ESBL in cattle, Figure 2 shows all countries. Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Italy, Netherlands, Portugal, Slovakia, Spain, Sweden, Switzerland, Turkey and United Kingdom, presented at least one report of E-ESBL in cattle (Aslantaş et al., 2017; Briñas et al., 2005; Dolejska et al., 2011b; Duse et al., 2015; Hordijk et al., 2013c; Hunter et al., 2010; Kjeldsen et al., 2015; Kmet and Bujňáková, 2018; Michael et al., 2017; Páivärinta et al., 2016; Pardon et al., 2017; Ramos et al., 2013; Stefáni et al., 2014; Toth et al., 2013; Valat et al., 2016; Zurfluh et al., 2015). CTX-M-1 was described in 14 of the 16 countries with E-ESBL in cattle, CTX-M-15 present in 7, CTX-M-14 in 6 and CTX-M-3 and SHV-12 in 5 (Aslantaş et al., 2017; Briñas et al., 2005; Dolejska et al., 2011b; Duse et al., 2015; Gay et al., 2018; Haenni et al., 2014; Hordijk et al., 2013b; Hordijk et al., 2013c; Hunter et al., 2010; Kjeldsen et al., 2015; Kmet and Bujňáková, 2018; Michael et al., 2017; Páivärinta et al., 2016; Pardon et al., 2017; Pehlivanoglu et al., 2016; Ramos et al., 2013; Timofte et al., 2014; Toth et al., 2013; Valat et al., 2016; Zurfluh et al., 2015).

Germany presented the description of CTX-M-1, CTX-M-1/61, CTX-M-2, CTX-M-3, CTX-M-14, CTX-M-15, CTX-M without the variant description (CTX-M), SHV-12, TEM-52 and E-ESBL without the description or detection of beta-lactamase (ND-ESBL) described in E. coli and Salmonella enterica from faecal and clinical samples (Dahms et al., 2015; Friese et al., 2013; Michael et al., 2017; Wieler et al., 2011; Wu et al., 2013). CTX-M-1, CTX-M-3, CTX-M-14, CTX-M-15 and SHV-12 have already been reported in E-ESBL in humans in Germany associated with infections (Gerhold et al., 2016; Mshana et al., 2009; Schmitt et al., 2007).

The Netherlands, German neighbours, also presented high diversity and number of reports of E-ESBL in cattle. There were identified CTX-M-1, CTX-M-2, CTX-M-2/97, CTX-M-8, CTX-M-9, CTX-M-14, CTX-M-15, CTX-M-22, CTX-M-32, CTX-M-55, CTX-M-65, CTX-M-79, CTX-M, SHV-12, SHV without description of variant (SHV), TEM-20, TEM-52, TEM-190 and ND-ESBL, all of them described in faecal E. coli. CTX-M-1, CTX-M-2, CTX-M-14, CTX-M-15, SHV-12 and TEM-52 have already been described in E-ESBL of human (faecal and hospital) origin in the Netherlands (Naïemi et al., 2006; Overdevest et al., 2011).

The biggest European cattle producer, France, including 2 French departments in Africa (Mayotte and Réunion) has reported E-ESBL in cattle with CTX-M-1, CTX-M-3, CTX-M-14, CTX-M-15, CTX-M-32, CTX-M, SHV-12, TEM-52, TEM-71 and TEM-126 reported in E. coli and K. pneumoniae of faecal and clinical origin. All of the described beta-lactamases (CTX-M-1, CTX-M-3, CTX-M-14, CTX-M-15, CTX-M-32, CTX-M-57, CTX-M-57, CTX-M, SHV-12, TEM-52, TEM-71 and TEM-126) in cattle have been reported in E-ESBL from humans of hospital origin in France (De Champs et al., 2004; Robin et al., 2017).

The United Kingdom was the European country with the highest number of reported CTX-M variants. The CTX-M-1, CTX-M-3, CTX-M-14, CTX-M-15, CTX-M-15/28, CTX-M-17/18, CTX-M-20, CTX-M-32, CTX-M, SHV-12 and ND-ESBL were reported in E-ESBL in cattle. E. coli and K. pneumoniae were the species that harbour the genes and these are of...
faecal and clinical origin. CTX-M-3, CTX-M-14, CTX-M-15, CTX-M-17/18 and SHV-12 have already been described in humans in E-ESBLs (Batchelor et al., 2005; Doumith et al., 2012).

Switzerland presented E-ESBL in cattle with CTX-M-1, CTX-M-14, CTX-M-15, CTX-M-117, CTX-M, TEM-186 and ND-ESBL (Geser et al., 2011, 2012a; Reist et al., 2013; Zurfluh et al., 2015). They were reported in 3 species: *E. coli*, *C. youngae* and *E. cloacae*. All reports were of faecal origin, with the exception of 1 case of mastitis (CTX-M-14) (Geser et al., 2012a). E-ESBL of human origin have been reported to harbour CTX-M-1, CTX-M-15 and TEM-24 in Switzerland (Geser et al., 2012b).

CTX-M-1, CTX-M-15 and TEM-24 were described in E-ESBL in cattle in Italy. Reported in *K. pneumoniae* (mastitis) and *K. ozaenae* (faecal carriage). The three types of ESBL described in cattle, CTX-M-1, CTX-M-15 and TEM-24, have also been described in human clinical isolates (Mugnaioli et al., 2006; Perilli et al., 2011).

Turkey is the second largest cattle producer in Europe and presented E-ESBL in cattle with CTX-M-1, CTX-M-3, CTX-M-15, SHV-5, SHV-12 and OXA-10 in *E. coli*, *C. freundii* and *C. brakii* of faecal origin (Aslantaş et al., 2017; Kucukbasmaci et al., 2008; Pehlivanoglu et al., 2016). CTX-M-1, CTX-M-3, CTX-M-15, SHV-5 and SHV-12 were reported in human clinical isolates in Turkish hospitals (Gur et al., 2008; Tasli and Bahar, 2005).

The Nordic countries have few reports and diversity of beta-lactamases, with E-ESBL in cattle harbouring CTX-M-1 in Denmark and Finland and CTX-M-1 and CTX-M-15 in Sweden all in *E. coli* and of intestinal origin (Duse et al., 2015; Kjeldsen et al., 2015; Päivärinta et al., 2016). When analysed the description in E-ESBL of human origin, CTX-M-1 has been described in Denmark, Finland and Sweden and CTX-M-15 in Sweden (Brolund et al., 2014; Forssten et al., 2010; Jakobsen et al., 2015).

In the Iberian Peninsula, Spain and Portugal also presented E-ESBL in cattle, with descriptions on Spain of CTX-M-1, CTX-M-55 and ND-ESBL and in Portugal of CTX-M-1 and CTX-M-32 (Brinas et al., 2005; Hernandez et al., 2017; Ramos et al., 2013). The descriptions in both countries were in *E. coli*, but in Spain they were of faecal and clinical

![Figure 4. Map of South America illustrating the countries with description of E-ESBL in cattle and the diversity of beta-lactamases presented.](image-url)

J. Dantas Palmeira, H.M.N. Ferreira Heliyon 6 (2020) e03206
origin and in Portugal only faecal. CTX-M-1 has already been described in E-ESBL in human in Spain and CTX-M-1 and CTX-M-32 in Portugal (Fernandes et al., 2014; Novais et al., 2007). CTX-M-1 was described in Hungary, Czech Republic and Slovakia and CTX-M-14 in Belgium in E-ESBL in cattle. All in E. coli and with faecal and clinical origins (Dolejska et al., 2013; Kmet and Bujnáková, 2018; Pardon et al., 2017; Toth et al., 2013). In E-ESBL of human origin, CTX-M-1 has already been reported in Hungary, Czech Republic and CTX-M-14 in Belgium (Dolejska et al., 2013; Ebrahimi, 2016; Rodriguez-Villalobos et al., 2011).

4. North America

In North America only 2 countries registered E-ESBL description in cattle, Canada and the United States, the last one being the world’s largest cattle producer (USDA et al., 2017). CTX-M-15, CTX-M-32 and CTX-M-65 were the only beta-lactamases described in both countries, the Figure 3 shows the complete described ESBL from cattle in the North America (Cormier et al., 2016; Mir et al., 2016; Poole et al., 2017; Tate et al., 2017; Wittum et al., 2010). CTX-M-1, CTX-M-14, CTX-M-15 and CTX-M-65 were reported in E-ESBL isolates from humans (Chen et al., 2014; Li et al., 2015; Tate et al., 2017; Wang et al., 2013).

CTX-M-1, CTX-M-2, CTX-M-14, CTX-M-15, CTX-M-24, CTX-M-27, CTX-M-32, CTX-M-55, CTX-M-65, CTX-M-115, CTX-M-172, CTX-M, SHV-2 and ND-ESBL were described in E-ESBL in cattle in Canada, which was the country where the largest variety of CTX-M’s types were described (Awosile et al., 2018; Cormier et al., 2016; Lussier, 2010). All E-ESBLs were E. coli of faecal origin. In E-ESBL of human origin in Canada were detected similarly to cattle the CTX-M-2, CTX-M-15, CTX-M-24, CTX-M-27, CTX-M-55 and SHV-2 (Denisuil et al., 2013, 2015; Peirano et al., 2010; Pitout et al., 2008).

5. South America

In South America E-ESBL is still poorly described, being few and incomplete, from the molecular point of view, the reports of E-ESBL in cattle in the countries of this continent. Only Brazil, Chile and Peru present reports of E-ESBL in cattle. Figure 4 shows what E-ESBL has already been described in these countries.
Brazil is the world’s second largest cattle producer and the world’s second largest exporter of cattle (USDA et al., 2017). The presence of E-ESBL in cattle with CTX-M-2, CTX-M-15, CTX-M, SHV and ND-ESBL has already been described in the country (Nóbrega et al., 2013; Palmeira et al., 2018; Santos, 2006; Sartori et al., 2017). Originated from mastitis or with faecal origin in E. coli and K. pneumoniae. There are several reports in human clinical E-ESBL of CTX-M-2, CTX-M-15, CTX-M and SHV in Brazil (Sampaio and Gales, 2016).

Chile and Peru describe the presence of E-ESBL, but not described the enzymes responsible for ESBL phenotype. These reports were in E. coli in mastitis in Chile and in E. coli and E. cloacae of faecal origin in Peru (Gonzalez, 2006; Mendoza, 2017). Both countries have reports of E-ESBL in humans (Colquechagua Aliaga et al., 2015; Hernandez et al., 2013).

6. Asia

The second continent with the highest number of countries reporting E-ESBL in cattle is Asia, which shows description of E-ESBL in 13 countries (China, Hong Kong, India, Indonesia, Iran, Israel, Japan, Lebanon, Malaysia, Saudi Arabia, South Korea, Thailand and Taiwan), highlighting China and India which are the fourth and fifth largest cattle producers in the world (Adler et al., 2015; Ali et al., 2017; Barzan et al., 2017; Diab et al., 2016; Hassan et al., 2015; Hinthong et al., 2017; Ho et al., 2015; Kamaruzzaman, 2015; Koovapra et al., 2016; Ohnishi et al., 2013a; Su et al., 2016; Sudarwanto et al., 2016; Tark et al., 2017). They have different roles in the import and export scenario, as India is the world’s largest exporter of cattle and China the largest importer, since its internal production is not sufficient for internal consumption (USDA et al., 2017). Figure 5 shows the countries and the diversity of beta-lactamases found in each of them.

China presents a description of E-ESBL in cattle harbouring CTX-M-1, CTX-M-2, CTX-M-14, CTX-M-15, CTX-M-17, CTX-M-28, CTX-M-55, CTX-M-65, CTX-M-88, CTX-M-98, CTX-M-102, CTX-M-103, CTX-M-123, CTX-M and SHV-12. All descriptions were in E. coli and faecal origin and mastitis (Ali et al., 2017; Yang et al., 2018; Zheng et al., 2019). CTX-M-3, CTX-M-14, CTX-M-15, CTX-M-55 and SHV-12 were described isolated from E-ESBL of human origin in China (Hu et al., 2013; Tian et al., 2012).

In India CTX-M-15, CTX-M-63, CTX-M, SHV-180, SHV and TEM in E-ESBL from cattle have already been described. Faecal origin and mastitis, being detected in E. coli and K. pneumoniae (Borah et al., 2014; Das et al., 2017; Koovapra et al., 2016). The presence of CTX-M-15 and SHV in E-ESBL in India has been reported in humans (Hawkey, 2008).

Japan and South Korea, the 3rd and 4th largest world importers of cattle, presented E-ESBL in cattle, respectively, with CTX-M-1, CTX-M-2, CTX-M-14, CTX-M-15 and SHV-11 and CTX-M-1, CTX-M-3, CTX-M-14, CTX-M-15, CTX-M-32, and CTX-M. These were detected in faecal E-ESBL and clinical in the animals and in Japan in E. coli, K. pneumonia, K. oxytoca, C. freundii, C. koseri, E. cloacae and E. aerogenes and in South...
Korea only in E. coli (Ohnishi et al., 2013a, b; Shiraki et al., 2004; Tamang et al., 2013a, b; Tark et al., 2017). In Japan CTX-M-14, CTX-M-15 and SHV-11 have been described in E-ESBL of human origin (Kuroda et al., 2012; Saito et al., 2014). The CTX-M-3, CTX-M-14, CTX-M-15 and CTX-M-32 beta-lactamases have already been described in E-ESBL of human origin in South Korea (Lee et al., 2009).

Hong Kong and Taiwan presented an E-ESBL profile in cattle only with reports of beta-lactamases of the CTX-M type. Hong Kong with CTX-M-3, CTX-M-14, CTX-M-28, CTX-M-55, CTX-M-98, CTX-M-123, CTX-M-132 and CTX-M (Duan et al., 2006; Ho et al., 2011, 2013, 2015). Taiwan already has CTX-M-14, CTX-M-15 and CTX-M-55 (Su et al., 2016). All in E. coli of faecal origin and mastitis. In Hong Kong the E-ESBL description of human origin has been reported well for CTX-M-14 and in Taiwan for CTX-M-14 and CTX-M-15 (Yan et al., 2006; Yeung, 2011).

Indonesia, Malaysia, and Thailand reported E-ESBL in cattle, respectively, for CTX-M-1 and CTX-M-9; CTX-M; and TEM and ND-ESBL. All in E. coli of origin in mastitis or faecal (Hinthong et al., 2017; Kamaruzaman, 2015; Sudarwanto et al., 2016). In humans, reports of E-ESBL have been described for CTX-M-1 in Indonesia, CTX-M in Malaysia and ND-ESBL in Thailand (Bagus Wasito et al., 2017; Ho et al., 2012; Kiratesis et al., 2008).

In the Middle East region there is a description of E-ESBL in cattle in Saudi Arabia (CTX-M), Iran (ND-ESBL), Israel (CTX-M-15, CTX-M, SHV and ND-ESBL) and in Lebanon (CTX-M-15). They were identified in E. coli and K. pneumoniae in faecal samples (Adler et al., 2015; Barzan et al., 2017; Diab et al., 2016; Hassan et al., 2015; Lifshitz et al., 2018). All E-ESBL profiles in cattle described above in these countries are also found described in humans (Bazzaz et al., 2009; Chmelitsky et al., 2005; Hassan and Abdalhamid, 2014; Moubareck et al., 2005).

7. Africa

In Africa, only 6 countries presented reports of E-ESBL in cattle. They were Egypt, Madagascar, Nigeria, South Africa, Tanzania and Tunisia (Braun et al., 2016; Gay et al., 2018; Iweriebor et al., 2015; Mkala and Azizi, 2017; Olowe et al., 2015; Saidani et al., 2018; Seni et al., 2016). There are not numerous nor descriptive reports on this continent. They are also not very prominent countries within the world economic cattle cycle, highlighting only Egypt which is the 8th biggest importer of cattle in the world (USDA et al., 2017). Figure 6 shows the countries with E-ESBL reported in cattle and what beta-lactamase type has been described in them.

In Egypt E-ESBL was described in cattle harbouring CTX-M-9, CTX-M-15, SHV-12, SHV-28, TEM and OXA-30. Described in E. coli, K. pneumoniae, K. oxytoca, E. cloacae and S. marcescens of faecal origin and mastitis (Ahmed and Shimamoto, 2011; Braun et al., 2016). There are reports in human E-ESBL also with CTX-M-9, CTX-M-15 and SHV-12 (Fam et al., 2011; Hamdy Mohammed et al., 2016; Newire et al., 2013).

South Africa (CTX-M), Madagascar (CTX-M-15), Nigeria (CTX-M and ND-ESBL), Tanzania (CTX-M-15) and Tunisia (CTX-M-15) also presented reports of E-ESBL in cattle. The reports were E. coli, Klebsiella sp, Salmonella sp, P. mirabilis, P. vulgaris, Providencia sp e Shigella spp (Gay et al., 2018; Iweriebor et al., 2015; Ogefere et al., 2017; Olowe et al., 2015; Saidani et al., 2018; Seni et al., 2016). In all countries the origin was faecal (except Tunisia, with mastitis also). All types of descriptions presented in these 5 countries for E-ESBL in cattle also present reports in humans (Abbassi et al., 2008; Iroha et al., 2012; Manyahi et al., 2017; Ouedraogo et al., 2016).
8. Oceania

In Oceania as one might imagine, due to its size and number of countries, there exist few reports of E-ESBL in cattle production. The only country with reports is Australia, which is the 6th largest world producer country and the 3rd biggest exporter (USDA et al., 2017). Figure 7 shows the countries with the E-ESBL description in cattle and what ESBL type has been described in them.

Australia presented a description of CTX-M-9 and CTX-M-14 in E-ESBL in cattle. The description was carried out in clinical isolated and in E. coli and in S. enterica (Abraham et al., 2015; Sparham et al., 2017). Both variants, CTX-M-9 and CTX-M-14, have already been described in human clinical isolates in Australia (Zong et al., 2008).

9. Conclusion

E-ESBL are a threat to human health and are now scattered around the world in intestinal colonization and clinical processes of cattle in Europe, the Americas, Asia, Africa and Oceania. These are described in 6 of the 7 major world cattle producers and certainly these E-ESBLs are contributing to the circulation of these and the ESBL genes through the ecosystems. A circulation that does not only concern the internal level of each country, since the circulation trade of cattle and their derivatives between countries is increasing, with E-ESBL being found in the animals of the world’s 5 largest meat exporters.

Further studies in the various areas of each country, as well as in other countries without data, are necessary for a better understanding of the presence and circulation of these E-ESBL through cattle and the food chain to assist in the implementation of measures to help in the surveillance and control of the E-ESBL dissemination and propagation.

Declarations

Author contribution statement

Josman Dantas Palmeira, Helena Maria Neto Ferreira: Analyzed and interpreted the data; Wrote the paper.

Funding statement

This work was supported by a scholarship from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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