Assessment of risk for antibiotic residues in milk of dairy livestock: a meta-analysis over the last decade

Zaira Kabdullina1,2*, Gaukhar Konuszpayeva1,2, Dariga Utemuratova1,2, Nurlan Akhmetzadykov2, and Farida Amutova1,2

1Al-Farabi Kazakh National University, Almaty, 050040, Kazakhstan
2Antigen LLP, Scientific and Production Enterprise, Almaty Region, 040905, Kazakhstan

Abstract. Nowadays, different types of antibiotics are being widely used in livestock for therapeutic purposes to treat infections. Significant quantities of them are excreted and remain in produced food items, including milk. This indicates improper use of antibiotics which may have serious consequences for human health. This comprehensive review was conducted with the aim to summarize existing knowledge about evaluation of antibiotic residues in milk of different livestock animals. This review involves 35 articles retrieved from PubMed, Google Scholar, ScienceDirect and Web of Science databases published from 2010 to 2023 and compares on the group of antibiotics identified, type of milk selected and various methods that were applied to undertake the research. Results showed that cow milk is the most intensively examined milk type (88.6%), whereas others, namely goat, camel, buffalo and sheep are less investigated on antibiotic residues. Among the techniques, chromatographic is revealed to be the most common due to its significant advantages over other methods. In addition, it was concluded that tetracyclines with the share of 85.6% are the group of antibiotics that is the most frequently studied in research articles.

1 Introduction

Milk is considered as an essential food to support the functions of human organisms across the globe. As there is a wide range of choice on the sources, people tend to devour various types of milk. Cow milk is considered to dominate the global milk industry (85% of milk produced in the world) being the most commonly consumed milk type. Buffalo milk is in the second position with around 11%, followed by goat (3.4%), sheep (1.4%) and camel milk (0.2%) [1]. Various antibiotics are actively used in agriculture in order to increase the shelf life of final food products, to stimulate the growth of healthy animals and to suppress pathogens in case of detection of a disease in other animals of the herd. It was estimated

* Corresponding author: zaira01211@gmail.com

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that antibiotic use in agriculture accounts for 73% of worldwide antibiotic application. Scientists predict that by 2030, sales of antibiotics in livestock production will rise by 11.5% [2].

The hazard of using antibiotics is due to the fact that entering the human body through food in small quantities, antibiotics trigger the mechanism of resistance to them and when they are needed to treat diseases, the antibiotics stop functioning. After antibiotic treatment a withdrawal period is mandatory to ensure an excretion of residues till a safe concentration. In order to prevent unwanted exposure, it should be lower or equal to the Maximum Residue Limit (MRL), which is a legal unit for the maximum accepted quantity of veterinary drugs in food products [3].

Antimicrobial resistance (AMR) has become a serious and growing threat to public health, food safety with significant associated economic consequences and global measures are being taken to tackle the issue. The “One Health” approach is central to the UN strategy to combat AMR [4], and since 2013, work has been underway to implement the global goal of reducing the use of antibiotics in food production and limiting the use of antibiotics important for human medicine in animals.

Therefore, this study was conducted with an aim to summarize existing knowledge about evaluation of antibiotic residues in milk of different livestock animals.

2 Materials and methods

The comprehensive search of previously published relevant research papers was conducted in databases as PubMed, Science Direct, Web of Science and Google Scholar both in English and Russian languages. Primarily, the request was based on the multiple combination of keywords (antibiotic residues, milk, tetracycline, penicillin, detection). Further, the snowball method, concerning the use of a reference list of selected articles in order to find additional studies on the same theme, was applied. Following the search, papers were revised and sorted out on the inclusion criteria. The original studies published in the period of time from 2010, having access to full-text articles and including analytical methods with quantitative results were selected.

A total of 35 research articles meeting aforementioned inclusion criteria were finally selected. They were analyzed based on the year of publication, geographical location, milk type, group of detected antibiotics and analytical techniques in experimental design. All the retrieved data was collected in a summary table and was analyzed in detail in each category. Afterwards, the gathered information was summarized in the form of narrative synthesis.

3 Results and Discussion

Concerning the country-wise analysis, it can be observed from the graded map (Fig. 1 A) that a higher amount of research was undertaken in developing countries rather than developed countries including India which is ranked 1st in the global milk production [5]. The majority of papers were published in Southwest, south Asia and north Africa countries, such as Iran and India with the highest number of 4 and 5, respectively. In contrast, only 1 publication was accomplished in 11 countries, particularly, Kazakhstan, Egypt, Canada, Sudan, Saudi Arabia, Romania, Kenya, Kosovo, Nigeria, Somalia and Nepal.

Figure 1 B represents the number of studies performed during the selected period of time, from 2010 till 2023. The overall trend shows that year after year more research is being done, thus increasing the scientific importance of the issue. Among the papers, the
largest number was published in 2021, followed by 2018 at 5 articles and no studies were published in 2012.

Fig. 1. Key findings. A) Geographical distribution of research. B) Timeline analysis. C) Types of milk samples.

Researchers might have been guided by comprehensive factors, concerning the availability, consumption rate, social and economic significance of milk types while selecting the paramount one for a study over others. A total of 5 origins of milks have been differentiated (Fig. 1 C), namely cow, buffalo, camel, sheep and goat. Some of the works were intended to investigate several milk types simultaneously. A substantial share of studies, 31 (88.6%) used cow milk and in 27 of them cow milk was the only milk type of interest, whereas other types had significantly much lower figures. Goat - 6, camel and sheep with identical results - 4 and only 1 article was accomplished to detect antibiotics in buffalo milk.

The selected articles were categorized by 6 classes of antibiotics based on the chemical structure, namely Sulfonamides, Quinolones, β-lactams, Tetracyclines, Macrolides, Aminoglycosides (Fig. 2). The majority of articles investigated a wide range of antibiotics, not a certain class of them. Tetracyclines are the most frequently detected at 85.6% of studies. The second most common group, β-lactams were the main focus of 24 articles, followed by Quinolones - 10, Aminoglycosides - 9 and Macrolides - 7. However, the data indicated that the Sulfonamides were mentioned only in 3, being the least encountered antibiotic type.

Different techniques were applied in the studies that were sorted out on the basis of nature into 4 categories: Chromatographic, Immunological, Microbiological and Various that are shown in Figure 3. 82.9% of articles are based only on 1 particular type, whereas the rest used the combination of them to figure out the most optimal method for antibiotic detection. Chromatography is the most frequent as it was common for 17 works (48.6%), while immunological methods including ELISA, Beta Star Combo were applied in 10
research, followed by microbiological having the score of 7. There were found other techniques that cannot be categorized into any of these groups, though they were mentioned in 6 articles.

![Fig. 2. Various classes of detected antibiotics in milk.](image)

**Table 1.** Methods applied to detect antibiotic residues in milk samples.

<table>
<thead>
<tr>
<th>Analysis type</th>
<th>Detection technique</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Chromatographic</td>
<td>HPLC, UHPLC, TLC, LC</td>
<td>[6], [8], [9], [10], [11], [12], [13], [14], [18], [22], [23], [26], [28], [29], [30], [31], [35]</td>
</tr>
<tr>
<td>2 Immunological</td>
<td>EIA, ELISA, Charm MRL test, Beta Star Combo, SNAP</td>
<td>[9], [13], [15], [18], [20], [21], [32], [38], [39], [40]</td>
</tr>
<tr>
<td>3 Microbiological</td>
<td>MIA, Copan test, ECLIPS 50 kit, Premi test kit</td>
<td>[7], [14], [16], [17], [24], [25], [33]</td>
</tr>
<tr>
<td>4 Various</td>
<td>Delvotest, Acidification test</td>
<td>[21], [22], [27], [34], [36], [37]</td>
</tr>
</tbody>
</table>

**4 Conclusion**

The presented review has given information and a comprehensive view on the worldwide situation of the research in the field of antibiotic residue detection in milk samples from all dairy animals. Because of the importance of decreasing milk consumption with antibiotic residues on human health in the frame of One Health movement more research works are being carried out across the globe. Year by year the essence of consuming organic and not contaminated milk is being taken into more consideration. Among the groups of antibiotics, the most used type is tetracyclines for dairy animals over other groups of antibiotics such as Sulfonamides, Quinolones, β-lactams, Macrolides and Aminoglycosides. In addition, chromatography technique can be considered the most effective and trustworthy method as it allows the detection of the majority of antibiotics widely applied in livestock with the minimum error and trace quantity even at the limited concentration. Key findings of the
study are that in identifying the level of contamination by antibiotics not significant attention is paid to other types of milk which are also widely consumed as cow milk. Therefore, these insights can be implemented in the nearest future to investigate more of other milk types, including camel, sheep or goat milk for antibiotic residues based on the foundation of this work for adapted technologies of production of organic milks of non-bovine milk taking into account the withdrawal period of antibiotics. Implementation of such technologies will conduct better quality life of consumers in different environments with local production of other dairy animals.

Conflict of interest

The authors declare no conflict of interest.

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Authors' contribution


References

   https://doi:10.22004/ag.econ.289000
   https://doi:10.3390/antibiotics9120918
   https://doi.org/10.14202/vetworld.2022.662-671
4. FAO, VMD. Tackling antimicrobial use and resistance in food-producing animals. pp. 70 (2022)  
   https://doi.org/10.4060/cc0927en
   https://doi:10.17485/iijst/2014/v7sp5.1
   https://doi:10.5455/ajvs.91952


