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Assessing the Risk of Antibiotic Residues in Milk Produced in the Republic of Armenia

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ABSTRACT

This research sets out to assess both the antibiotic exposure via milk produced in the Republic of Armenia and the associated human health risks. As established, the milk of domestic production contains residual antibiotics (streptomycin, chloramphenicol, tetracyclines). The estimated daily intake (EDI) and the margin of exposure (MOE) for the antibiotics identified upon this research were assessed. It has been indicated that for the population of Yerevan, the daily intake of antibiotics via milk does not exceed the acceptable daily intake (ADI). Moreover, the derived MOE values point to the absence of health risks associated with shop-bought milk.

Introduction

Milk and dairy manufacturing is one of the relatively developed branches in Armenia's agriculture and food industry (FAO, 2012). According to the data of Statistical Committee, in 2019, 667.9 thousand tons of milk were produced with 242 kg average annual per capita milk consumption (Armstat, 2019). It is well-known that milk and dairy products have a high nutritional value, contain vitally essential proteins, fats, vitamins, mineral salts, microelements, and, thus, are staple food in the consumer basket (Popescu, et al., 2019, Priyanka, et al., 2017). However, some studies suggest that, besides useful elements, milk may also contain harmful substances and antibiotics in particular (Bahmani, et al., 2020). The latter are known as antimicrobial medicines of natural or semi-synthetic origin widely applicable for different human and animal diseases to prevent and cure (Bacanli and Başaran, 2019, Bingyao, et al., 2019). Thus, the chief cause for antibiotics to enter milk content is the antibiotic treatment of dairy cattle. It is also a fact that, being heat resistant, antibiotic agents are not destroyed even when exposed to high temperatures when processing food (Hassan, et al., 2020). So, eating food contaminated with residual antibiotics may cause serious health effects: different allergic responses, insensitivity or super-susceptibility to antibacterial agents, disturbance of intestinal microflora and so on (Zhang, et al., 2010, Zhao, et al., 2021).

The issue of antibiotics in food and the health effects these

agents produce has been in the spotlight of many competent international institutions, such as the World Health Organization (WHO), Food and Agriculture Organization (FAO), European Food Safety Authority (EFSA), US Food and Drug Administration (FDA), who often touch upon these topics in their reports (WHO, 2014, EFSA, 2012, US FDA, 2015, FAO, 2018). These topics are a concern to both developed and developing nations. One should stress that in the developing countries, including Armenia, scientifically robust data on antibiotic agents in foods consumed are yet too scarce to meet food safety challenges of the day. So, the main mission of this research was to fill up this information gap by adding newly generated food safety data to those currently available in Armenia.

Given the above, our research goal was to determine the presence of antibiotics (tetracyclines, streptomycin, chloramphenicol) in raw milk produced in Armenia and assess associated health risks exposure.

Materials and methods

Milk sampling and determining the presence of antibiotics

Raw milk was sampled in the frame of the program "Monitoring the Residues in Animal and Animal-Based Foods" implemented by Food Safety Inspectorate Body (FSIB) under the RA Government.

Milk samples were transported to RVSPCLS (Republican Veterinary-Sanitary and Phytosanitary Center of Laboratory Services, SNCO) at 4 ^{0}C to be then analyzed for residual tetracyclines, streptomycin and chloramphenicol. Prior to the analysis, the milk samples underwent pre-treatment in compliance with the methodical guideline on RIDASCREEN® enzyme immunoassay kits. The quantitative lab measurements of antibiotic residues were made by the enzyme-linked immunosorbent assay (ELISA).

The accuracy of testing results was verified through a high-performance liquid chromatography (HPLC) method.

Estimated daily intake (EDI) of antibiotics through milk

The daily intake of antibiotics through milk is estimated by the formula (1) as follows:

$$EDI = \frac{IR_{milk} \times C_{antibiotic}}{BW}, \quad (1)$$

where $\boldsymbol{IR_{milk}}$ is daily intake of milk, $\boldsymbol{C_{antibiotic}}$ – residual quantities of tetracyclines, streptomycin and chloramphenicol in the milk samples, ***BW*** - the average body weight, which is estimated as 65 kg for Armenia's adult population.

To specify the milk consumption data, we have surveyed females and males aged 18-65 using Food Frequency Questionnaire (FFQ). The survey was conducted among 400 Yerevanians in January-February, 2020. The survey data input and analysis were done through the SPSS program (SPSS Ins., version 22.0).

Margin of Exposure (MOE)

The margin of exposure was calculated with the formula (2):

$$MOE = \frac{HBGV}{EDI}, \quad (2)$$

where ***HBGV*** is a health-based guidance value. In this research we employed ADI (Acceptible Daily Intake) values as ***HBGV*** for tetracyclines and streptomycin equal to 0.03 and 0.05 mg/kg b.w., respectively (FAO, 1999), for chloramphenicol – RPA (Reference Point of Action) value - 0.0003 mg/kg b.w. (EFSA, 2018). ***MOE*** calculated for different substances may vary widely. Anyhow, low MOE - as compared with high MOE- is indicative of the higher risk (EFSA, 2012).

Results and discussions

The contents of antibiotics

The contents of tetracyclines, streptomycin and chloramphenicol identified in the milk samples are given in Table 1.

Technical Regulations of the Customs Union (TR CU 033/2013) and Commission Regulation (EU No 37/2010) ban on antibiotics in milk, meanwhile setting up the maximal threshold for their residual quantities.

Table 1. The contents of antibiotics in the studied milk samples*

N	Antibiotics	The contents of antibiotics (µ/kg)		
		Minimal	Maximal	Mean ± SD
1.	Tetracyclines	0.77	4.75	1.76 ± 1.09
2.	Streptomycin	94.19	519.72	209.27 ± 117.5
3.	Chloramphenicol	0.09	0.70	0.24 ± 0.19

Note: SD - standard deviation.

*Composed by the authors.

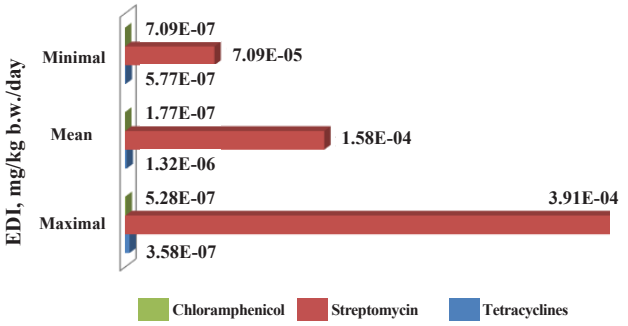

Figure 1. The estimated daily intake of antibiotics via milk by the adult population of Yerevan (*composed by the authors*).

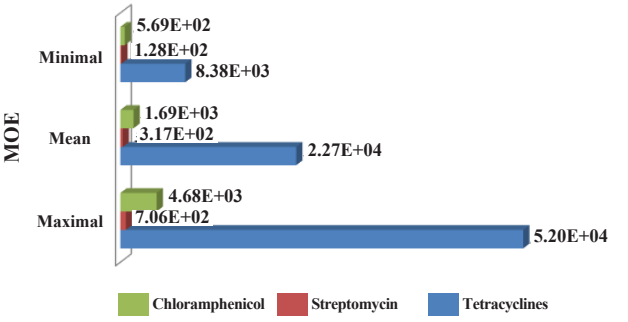

Figure 2. The margin of exposure to antibiotics (*composed by the authors*).

The results obtained have indicated that the contents of residual tetracyclines identified in the studied milk samples vary in the range of 0.77-4.75 μ/kg not exceeding however maximum residue limits – respectively 10 μ/kg and 100 μ/kg, as defined by Technical Regulations of CU and EU.

The mean residual content of streptomycin in the studied milk samples (209.27 μ/kg) exceeds the maximum residue limits - 200 μ/kg, whereas in some samples, its maximal contents overstep these limits several times.

Residual contents of chloramphenicol vary within 0.09 to 0.7μ/kg and exceed the allowable level set up by CU technical Regulation (CU TR 033/2013). This is evidence of the illegal use of this antibiotic.

Estimated daily intake (EDI)

Diet studies have indicated that for 2020 the average daily intake of milk in Yerevan is estimated as 0.049 kg/day. Data on the estimated daily intake of antibiotics via milk among the adult population of Yerevan are presented in Figure 1.

The next step in the research was collating the data obtained on EDI of antibiotics via milk (Figure 1) with the respective health-based guidelines values. The results obtained have indicated that EDI (estimated daily intake) values for streptomycin and tetracyclines-respectively 0-0.05 and 0-0.03 mg/kg/b.w./day - are consistent with those of ADI (acceptable daily intake) set up by international organizations (FAO, 1999).

Collation between the EDI values for the studied antibiotics indicate that they are significantly lower in case of chloramphenicol. It should be also mentioned that no health-based guidance value i.e. ADI is set up for chloramphenicol.

Margins of Exposure (MOE)

The MOE values calculated for assessing the risk of antibiotics for the adult milk consumers in Yerevan are given in Figure 2.

The calculated MOE values for the antibiotics identified in milk are rather high. Low MOE is known to indicate higher risks than high MOE does. MOE <10 denotes that risk exposure by the given substance is well concerning. The results derived from this research (Figure 2) point to the absence of the risk exposure to antibiotic identified in milk content.

Conclusion

In the result of the conducted research, it has been found out that in some samples of shop-bought milk of domestic production, two of three studied antibiotics - streptomycin and chloramphenicol residues - exceed the maximum residue limits. However, exposure to antibiotics via milk poses no health risks to adult milk consumers in Yerevan. And finally, the presence of banned antibiotics in the studied milk samples makes it urgent to improve the milk and milk-based produce quality and to develop control measures in milk producers nationwide, as well as to pursue research aimed at food-associated health risk identification.

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