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Determination of streptomycin residues in imported and locally produced honey in Kosovo

Adem Rama¹, Imer Haziri^{1*}, Iliriana Miftari¹, Afërdita Zuka², Blend Zhuri¹, Arlind Latifi¹, Drilon Hasani¹ and Fatgzim Latifi¹

Abstract

Although bee honey is considered an essential and healthy food for humans, honey can be affected by various contaminants, such as antibiotics, that can cause health problems for consumers. The objective of this study was to assess the occurrence of streptomycin residues in locally produced and imported bee honey, which was collected in 2017 from individual apiaries and retail markets in six different regions of Kosovo. In the present study, 155 bee honey samples were qualitatively screened by the enzyme-linked immunosorbent assay (ELISA) method using an I'screen STREPTO test kit (Tecna S. r. L., Trieste, Italy) as a simple and fast method. Descriptive statistics were used to outline the essential characteristics of the sample and mass; 29% of samples were contaminated with streptomycin at concentrations between 2.1-9.3 ug/kg, while 71% of the samples were found to be negative for streptomycin. Most of the samples with streptomycin residues were from the Ferizaj and Prizren regions. Based on these results, competent authorities should establish and maintain programs to continuously monitor honey to ensure that consumers in Kosovo receive risk-free honey. In addition, there is a pressing need for additional research to accurately assess other aspects of this problem and identify effective corrective actions that will reduce contaminants in bee honey.

Keywords: Honey, Streptomycin, ELISA, Public health, Kosovo

Introduction

Honey is a natural food product with high nutritional and therapeutic value, is produced by bees (*Apis mellifera*) and is a very popular food item for humans (Terzo et al. 2020; Kala et al. 2020). However, in addition to its high nutritional values, honey may also contain various contaminants, which can be a source of risk to consumer health. The most common contaminants found in bee honey are different antibiotics, pesticides, heavy metals, etc. (Irungu et al. 2016; Kumar et al. 2020; Ullah et al. 2022).

Beekeepers commonly apply antibiotics to eliminate diseases among honeybees. Researchers revealed that antibiotic residues in honey mainly originate from inappropriate beekeeping practices and not from the environment (Reybroeck 2018; Hermanns et al. 2020; Laconi et al. 2022). Moreover, some veterinary drugs used in beekeeping are suspected to cause certain types of cancer, teratogenicity, chromosomal abnormalities, and weakened immune systems in humans (Ribeiro et al. 2020; Rani et al. 2021). Some drugs have the potential to directly produce toxic reactions in consumers. Antibiotics can cause cutaneous eruptions, dermatitis, gastrointestinal symptoms, and anaphylaxis at very low doses (Menkem et al. 2019). Antibiotic residues that are consumed along with honey can lead to bacterial resistance in consumers, which makes treating

*Correspondence: imer.haziri@uni-pr.edu

¹ Department of Veterinary Medicine, Faculty of Agriculture and Veterinary, University of Prishtina "Hasan Prishtina", 10000 Prishtina, Kosovo
Full list of author information is available at the end of the article



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many infections in humans difficult (Pyun et al. 2008). Low dosages or inappropriate antibiotic prophylaxis in food animals (including bees) for long periods could result in antibiotic-resistant bacteria, which can be transferred from food to humans (Bacanli and Basaran 2019). However, treating honeybees with antibiotics is prohibited in the European Union (EU), and there have been significant advances in EU legislation concerning risk assessments. To date, no maximum residue levels (MRLs) have been established for antibiotics and sulfonamides in honey (European Union 2010), which theoretically means that the European Commission does not permit the use of antibiotics by beekeepers. Some countries, such as Switzerland, the UK, and Belgium, have established action limits (the maximum level of acceptable antibiotics in honey samples) for antibiotics in honey, which generally lie between 1.0 to 5.0 ug/kg for each antibiotic group.

Streptomycin (an antibiotic) is a protein synthesis inhibitor, and despite its toxicity, streptomycin is widely used in veterinary medicine to treat aerobic gram-negative bacterial infections (Araby et al. 2020; Anandabaskar 2021). Streptomycin is commonly used in apiculture for prophylactic treatments or to control bacterial brood diseases, such as European foulbrood and American foulbrood disease (Granja et al. 2009; Demirha and Demirha 2022). High concentrations of streptomycin may cause ototoxicity and nephrotoxic effects. However, regular consumption of streptomycin at low concentrations in foods may also cause allergies, destroy intestinal flora, and cause resistance to certain microorganisms (Cara et al. 2013; Ngangom et al. 2019).

Kosovo has suitable environmental conditions for practising beekeeping, such as its climate, relief, and abundance of honey-bearing plants, guarantying the production of good honey and beekeeping products (Panettieri 2013). Beekeeping is a viable business that significantly contributes to increasing and diversifying the incomes in many rural households in Kosovo (Mafred 2021). Currently, Kosovo has 6,453 beekeepers with 70,664 beehives that are distributed in Kosovo's territory, in which a bee community produces an average of 9.55 kg honey or 674 t/yr. In contrast, imports in 2014 were approximately 140 t/yr (Kosovo Agency of Statistics 2019). In addition to honey, other products are produced, such as pollen, wax, propolis, and bee's milk. (Mafred 2021).

Similarly, Kosovo also imports honey, but there is no standard to check the quality of imported honey. Based on our knowledge, there is no report on streptomycin contaminations in honey in Kosovo. Therefore, this research aims to determine the presence of streptomycin in honey produced in Kosovo and imported honey.

Materials and methods

Samples

One hundred fifty-five (155) honey samples were collected from different markets (local and imported honey) and beekeepers in six regions of Kosovo (Gjilan, Mitrovica, Peja, Prizren, Prishtina, and Ferizaj) between June and September 2017 (Fig. 1).

Sampling was performed according to EU requirements (European Union, 2006).

The local honey (131) was provided by beekeepers from several regions in Kosovo, while imported honey samples (24) were collected from retail markets. As suggested by the beekeepers, all honey samples were labelled either according to their botanical or geographical origin. The samples were stored at room temperature in the dark until analysis. One honey sample was checked and did not contain any of the targeted antibiotics

Antibiotic analysis by ELISA

The determination of streptomycin was performed by the enzyme-linked immunosorbent assay (ELISA) method using the I'screen STREPTO test kit (Tecna S. r. l., Trieste, Italy). Analyses were performed according to the test kit's instructions. The procedure was based on the binding of free antibiotics from samples and standard solutions to the anti-streptomycin antibodies during the first incubation. Any unbound substance was removed in a washing step. A second incubation was performed with a streptomycin-HRP conjugate, which covered all the antibody's remaining free binding sites. The bound enzyme activity was determined by adding a fixed amount of a chromogenic substrate. The enzyme converted the colourless chromogen into a blue product during the third incubation. The addition of the stop reagent led to a colour change from blue to yellow. The absorbance was measured by a microplate reader (Bio-Tek, USA) at 450 nm. The colour development is inversely proportional to the streptomycin concentration in the sample. The concentration of streptomycin was calculated from the calibration curve, which was obtained using six standards with the following concentrations: 0, 0.1, 0.25, 1, 5, and 20 ug/kg (Table 1).

Analytical sessions were compliant with assay specifications as follows: Mean B_0 absorbance; B/B_0 50% value; and CV% value related to standard duplicates mean. In our study, the recovery of streptomycin in spiked honey samples was found to be 84% (CV = 3.12), 92% (CV = 1.23) and 98% (CV = 1.03) for spiking concentrations of 20, 80, and 100 ug/kg, respectively. All experiments were performed in triplicate.

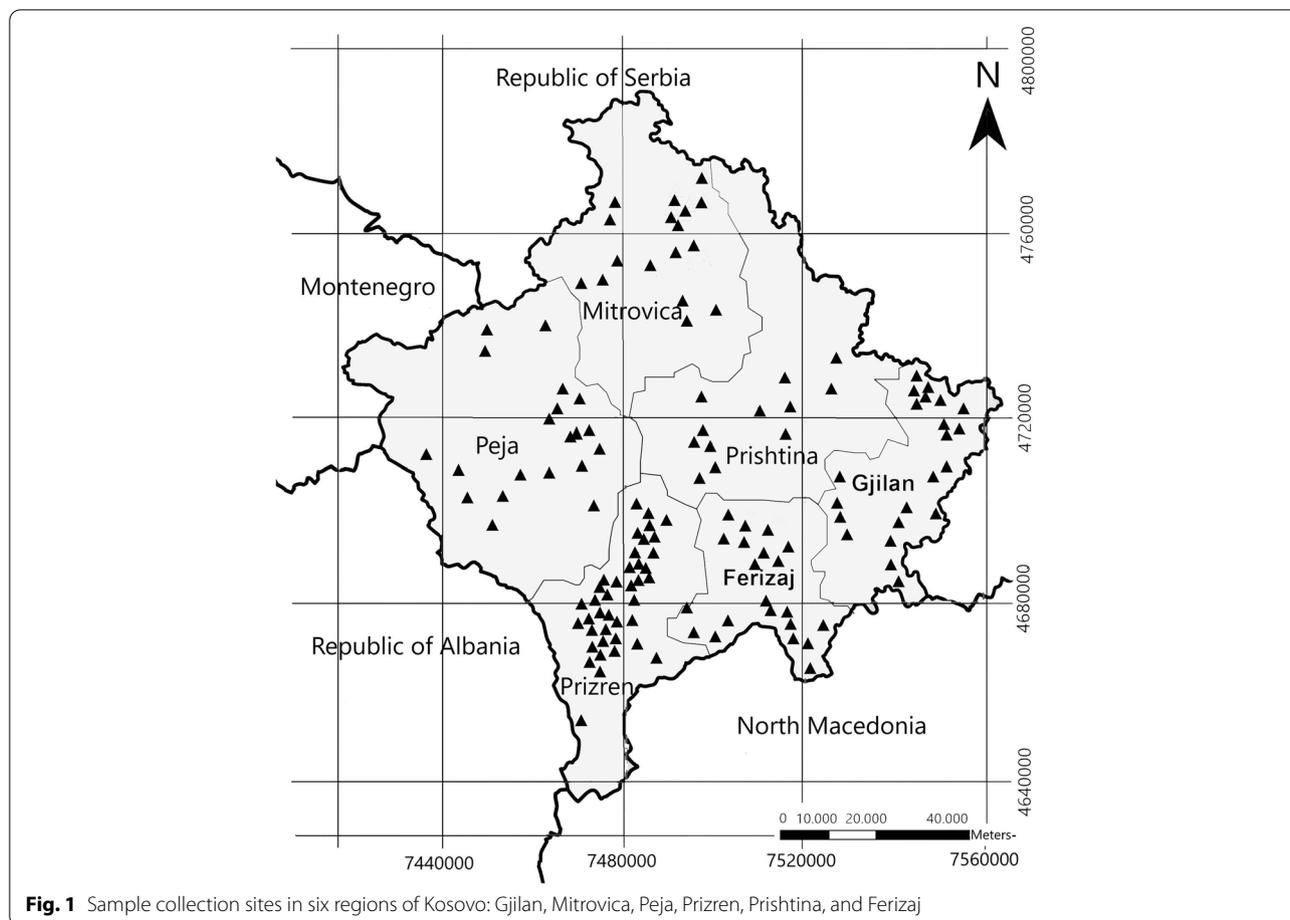


Fig. 1 Sample collection sites in six regions of Kosovo: Gjilan, Mitrovica, Peja, Prizren, Prishtina, and Ferizaj

Table 1 Obtained reference values of I’screen STREPTO

	Std 1	Std 2	Std 3	Std 4	Std 5	Std 6
Concentration (ug/kg)	0.0	0.1	0.25	1	5	20
B/B_0	100.0	83.0	70.8	47.6	23.8	13.7

Sample preparation

Streptomycin screening tests were performed at the National Institute of Public Health of Kosovo. Estimates of streptomycin quantities were performed using STREPTO I’screen enzyme immunoassay (Code AB650) at 0.0, 0.25, 1.5, and 20 ug/kg. The detection limit (LOD) for streptomycin is two 2 ug/kg.

Honey samples were prepared according to the manufacturer’s instructions. One gram of homogeneous honey sample was weighed, 19 ml of dilution buffer (1x) was added, and the honey was shaken or rotated until completely dissolved. The sample was filtered with Whatman N ° 1, and the dilution factor was 20. The samples were tested immediately after preparation.

Statistical analysis

Descriptive statistics are performed to provide an overview of all data. The final statistics were used to test hypotheses and evaluate parameters. Statistical analyses were performed using software version 21 of the Statistical Package for Social Sciences (SPSS, USA). Within the final statistics, Fisher analysis of variance (ANOVA) was performed to test the hypothesis of statistically significant differences in streptomycin concentration. In honey among the six regions and samples of imported honey. The T test was used for pairwise comparisons between the six regions. The significance level for the differences was set at $P < 0.05$, $P < 0.01$, and $P < 0.001$.

Results

In our validation tests, we spiked 40 honey samples (the sensitivity tests were performed twice 20 + 20) at the level of 5 µg/kg streptomycin, and we obtained a sensitivity of 97.5%. This means that in 97.5% of the samples were present streptomycin. Usually, that value has been reported as CCbeta (European Union, 2021). Moreover, the difference in B/B₀% of spiked samples vs. negative samples was 21 B/B₀%.

The average rate of streptomycin detection in the samples of locally produced honey and imported honey in the Kosovo market is shown in Table 2.

The mean concentrations of streptomycin in the locally produced honey and imported honey were 2.709 ± 0.227 ug/kg and 2.850 ± 0.559 ug/kg, respectively.

Most of the samples that contained streptomycin were found in the Ferizaj region (9/42.8%) with a concentration of 2.24-9.78 ug/kg and Prizren (13/33%) with a concentration of 2.2-6.82 ug/kg. In imported honey, the frequency of streptomycin was higher. Thus, 11 (45.8%) out of 24 samples had a concentration of 2.2-9.8 ug/kg (Table 3).

The descriptive statistics and the p values of the performed *t tests* for the differences in streptomycin concentration in bee honey among the six regions (Gjilan, Mitrovica, Peja, Prizren, Prishtina, and Ferizaj) and imported bee honey are shown in Table 4.

In the analysis of the variance of the concentration of streptomycin in bee honey among the six regions of Kosovo and imported bee honey, we observed that Prishtina had the highest concentration, followed by Ferizaj> Imported>Prizren,>Mitrovica> Peja, > Gjilan. The pairwise comparison presented in Table 4 shows that the concentration of streptomycin in the bee honey produced in the Gjilan region differs significantly from the bee honey produced in Prizren (*t* = 2.86; *p* = 0.005), Prishtina (*t* = 6.49; *p* = 0.000), Ferizaj (*t* = 6.58; *p* = 0.000), and the imported honey (*t* = 2.87; *p* = 0.005), but no significant differences in terms of streptomycin concentration were observed between Prishtina and Mitrovica (*t* = 1.81; *p* = 0.073) as well as Prishtina and Peja (*t* = 0.23; *p* = 0.816). Significant differences were observed between the Mitrovica, and Prishtina (*t* = 4.63; *p* = 0.000) , and between Mitrovica and Ferizaj (*t* = 4.37; *p* = 0.000) regions when a pairwise comparison was performed. The concentration of streptomycin in the bee honey produced in the Peja region differs significantly from the bee honey produced in Prizren (*t* = 2.51; *p* = 0.013), Prishtina (*t* = 6.18; *p* = 0.000), Ferizaj (*t* = 6.19; *p* = 0.000), and the imported honey (*t* = 2.56; *p* = 0.012). The statistically significant difference in terms of streptomycin concentration in bee honey was proven between Prizren and Prishtina (*t* = 4.74; *p* = 0.000) and Prizren and Ferizaj (*t* = 4.60; *p* = 0.000). Similar results were observed between Prishtina

Table 2 Occurrence of streptomycin antibiotic in commercial honey in Kosovo during 2017

Honey	Nr. of Samples	Nr. of samples containing streptomycine	Nr. of samples without streptomycin	Samples with streptomycin Mean ± SD
Local	131	34 (25.9%)	97 (74.1%)	2.709 ± 0.227
Imported	24	11 (45.8%)	13 (54.2%)	2.850 ± 0.559
Total	155	45 (29%)	110 (71%)	2.731 ± 0.210

Table 3 Distributions of streptomycin concentration (ug/kg) by regions detected in samples of domestic and imported honey during 2017

Regions	Total samples n	Samples with streptomycin present n (%)	Lower and upper Streptomycin contamination level (ug/kg)
Local			
Gjilan	22	2 (9.1)	6.92-9.32
Mitrovica	17	3 (17.6)	2.31-5.78
Peja	20	4 (20)	2.1-5.3
Prizren	39	13 (33.3)	2.2-6.82
Prishtina	12	3 (25)	4.38-8.78
Ferizaj	21	9 (42.8)	2.24-9.78
Imported	24	11 (45.8)	2.2-9.8
Total	155	45 (29.0)	2.1-9.8

Table 4 The differences in streptomycin concentration among the regions included in the study

Regions	Difference between regions	Mean Difference	SE of difference	T-Valeue	P- Valeue
r ₁ (n=22)	r2-r1	1.39	0.77	1.81	0.073
	r3-r1	0.17	0.74	0.23	0.816
	r4-r1	1.82	0.64	2.86	0.005
	r5-r1	5.56	0.86	6.49	0.000
	r6-r1	4.79	0.73	6.58	0.000
	r7-r1	2.021	0.70	2.87	0.005
r ₂ (n=17)	r3-r2	1.22	0.79	1.55	0.124
	r4-r2	0.43	0.69	0.62	0.537
	r5-r2	4.17	0.90	4.63	0.000
	r6-r2	3.40	0.78	4.37	0.000
	r7-r2	0.63	0.76	0.83	0.408
r ₃ (n=20)	r4-r3	1.65	0.66	2.51	0.013
	r5-r3	5.39	0.87	6.18	0.000
	r6-r3	4.62	0.75	6.19	0.000
r ₄ (n=39)	r7-r3	1.85	0.72	2.56	0.012
	r5-r4	3.74	3.79	4.74	0.000
	r6-r4	2.97	0.65	4.60	0.000
r ₅ (n=12)	r7-r4	0.20	0.62	0.32	0.749
	r6-r5	0.76	0.86	0.89	0.377
r ₆ (n=21)	r7-r5	3.54	0.84	4.19	0.000
	r7-r6	2.77	0.14	3.89	0.000

Note: Given characters denote: r-regions; r₁-Gjilan; r₂-Mitrovica; r₃-Peja; r₄- Prizren; r₅-Prishtina; r₆-Ferizaj; r₇- Imported. Significance of variations is denoted as follows: *P<0.05; **P<0.01; *** P<0.001.

and imported (t = 4.19; p = 0.000), as well as Ferizaj compared to imported bee honey (t = 3.89; p = 0.000).

Discussion

In our study, streptomycin was present in 25.9% of the locally produced honey and 45.8% of imported honey samples. These results are similar to the findings of some previous studies. In research done in Germany, 21% of samples contain streptomycin (Brasse 2001). These results are in parallel with the results found in our study. The presence of streptomycin in the honey samples may be due to inadequate use of streptomycin-based antibiotics, such as Fructocyn or Plantomicyn, by horticulturists in both countries to combat fire blight disease, which is a contagious disease that affects the apples and pears from which bees obtain nectar. Reybroeck (2003) monitored 248 samples of locally produced and imported honey on the Belgian market for residues of antibiotics in 2000-2001, and he reported that streptomycin was present in 4 (248) locally produced honeys. In Kosovo, for comparison, streptomycin was found in 34 (131) locally produced honeys. There is a significant difference between Kosovo (25%) and Belgium (1.6%) regarding the number samples containing streptomycin. In a study conducted in

Belgium, 38 (21%) out of 181 imported honey samples contain streptomycin (Van Bruijnsvoort et al. 2004). In our research, 45.8% of imported honey samples contain streptomycin. This high number of samples with streptomycin in Kosovo might result from the unsystematic control of food products that enter the country. While analysing honey with the ELISA method, Jiang et al. (2022) found an average streptomycin content of 15 ug/kg, which was much higher than our results (2.1-9.8 ug/kg). In a study conducted by Ağaoğlu et al. (2020) in Turkey, 60 honey samples were tested using the ELISA method, and 93.3% of the samples contain streptomycin at a concentration level of 0.19-22.71 ug/kg. In comparison, in our research, streptomycin was detected in 29% of the samples at a concentration level of 0.21-2.731 ug/kg. The results in Turkey were different from the results in our research. This may be because beekeepers in Turkey can use relatively sizeable amounts of antibiotics, given that in Turkey, there is an evident occurrence of bacterial diseases in beekeeping (Borum et al. 2015). The presence and concentration of streptomycin in both countries might result from the illegal and uncontrolled use of antibiotics by beekeepers or even from exposure of bees to water and food contaminated by antibiotics that farmers

used to treat various diseases. Zai et al. (2013) identified six contaminated antibiotic samples out of 100 analysed honey samples collected from Pakistani markets.

This percentage of streptomycin was lower than that of our findings (25.9% of locally produced honey and 45.8% of imported honey). This lower value of streptomycin in bee honey in Pakistan compared to that for Kosovo may be because beekeepers in Pakistan use different antibiotics against American foulbrood disease, and this practise is quite widespread in Pakistan (Anjum et al. 2015). Additionally, other antibiotics are used instead of streptomycin to treat bacterial infections in the Asian region (Kumar et al. 2020). There are few reports of antibiotics in honey in neighbouring countries, such as Serbia and Bosnia Herzegovina. Dugalić- Vrndić et al. (2005) analysed 100 honey samples in Serbia, of which 18 samples contain sulfonamide residues. In contrast, Dugalić-Vrndić et al. (2011) tested 65 honey samples and found residues of antibiotics and sulfonamide in 8 samples. Apić et al. (2015) examined 193 honey samples in Vojvodina. The presence of antibiotic residues in honey was observed in 5 out of 193 tested honey samples. Mujić et al. (2011) analysed the presence of antibiotic residues in 46 honey samples in Bosnia and Herzegovina, whereby no concentrations of antibiotics and sulfonamides were found. These studies indicate that antibiotics were not present in honey that was intended for human consumption.

Conclusions

Our results show that streptomycin was present in honey that was intended for human consumption in Kosovo. Using the ELISA technique, we analysed 155 honey samples that were produced in Kosovo and imported honey for the presence of the antibiotic streptomycin. 29% of 155 samples contain streptomycin at concentrations 2.1–9.3 ug/kg, while in 71% of the samples were not present streptomycin. Although limited by the region, significant residues of streptomycin were found in honey that are a concern for human health, prompting some recommendations for public authorities, veterinarians, beekeepers, and consumers. In addition to enforcing proper regulatory legislation and providing an adequately controlled sampling network, we must be able to provide adequate tools for food control with appropriate risk assessments that inspire consumer confidence. Competent authorities should establish and maintain ongoing monitoring programs to ensure that honey and its products are safe for Kosovar consumers. Furthermore, there is an urgent need for additional research to accurately assess other aspects of this problem and identify and develop effective corrective actions to reduce honey contaminants.

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Authors' contributions

Conceptualization A.R, I.H, and F.L; methodology, A.R, I.H, and F.L; software, A.R, I.H, and I.M; validating, A.R, I.H, and A.Z; formal analysis, A.R, I.H, A.Z, B.ZH, A.L, D.H, and F.L; investigation, A.R, I.H, and F.L; resources, A.R, I.H, and F.L; data curation, A.R, I. H, I.M, and F.L; writing original-draft preparation A.R, I. H, I.M, and F.L; writing-review and editing, A.R, I.H. A.Z, B.ZH, A.L, D.H, and F.L; visualization, A.R, I.H, and F.L; supervision, A.R, I.H, and F.L; project administration, A.R, I.H, and F.L; funding acquisition, A.R, I.H, I. M, and F.L; writing-review and editing in revision. All authors have read and agreed to the published version of the manuscript.

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Author details

¹Department of Veterinary Medicine, Faculty of Agriculture and Veterinary, University of Prishtina "Hasan Prishtina", 10000 Prishtina, Kosovo. ²National Institute of Public Health of Kosovo, 10000 Prishtina, Kosovo.

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