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Bozok Veterinary Sciences

2024; 5 (1)

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İçindekiler/Contents

(2024) 5,(1)

Araştırma Makaleleri/ Research Articles	Sayfa / Page
❖ **Dereli ÖN, Gulmez M, Yıldız Bayhan K, Üner S.** *Use of Raw, Thermized and Pasteurized Cow's Milk for Making Siirt Herby Tulum Cheese.*	**1-9**
❖ **Karadal F, Sakin-Şahin T, Bağcı C, Ertaş Onmaz N.** *Quality Characteristics of Raw Milk Samples Purchased from Automatic Milk Vending Machines in Niğde Province.*	**10-17**
Olgu Sunumu / Case Reports	
❖ **Erdogan S, Ak G, Erdogan H, Ural K.** *Clinical Efficacy of Bleomycin in Suspected Canine Papillomatosis: Case Report of Two Sibling Puppies.*	**18-22**
Derlemeler / Review Articles	
❖ **Yılmaz KB.** *Advancing Dairy Cattle Farming: Integrating Herd Management, Automation and Artificial Intelligence for Elevated Productivity and Sustainable Practices*	**23-30**
❖ **Uslu M ve Yazar E.** *Taylarda Rhodococcus Equi Enfeksiyonunda Antibiyotik Kullanımı.*	**31-34**

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Araştırma Makaleleri / Research Articles

Use of Raw, Thermized and Pasteurized Cow's Milk for Making Siirt Herby Tulum Cheese*

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Abstract: In this study, Siirt Herby Tulum Cheese was made from raw, thermized, and pasteurized cow milk collected from a farm. Production and packing were accomplished in under 24 hours. Pasteurization was performed at 72˚C for 1 minute, followed by termization at 68˚C for 1 minute. Cloth formation was done at 32˚C for 90 min. The clot was divided into 1x1x1 cm pieces, incubated for 45 min, and then filtered for 15 min. First, pressure was applied to the strained curd, which was then mixed with 1% salt and less than half the weight of milk for 12 hours. Sirmo (*Allium* sp.) was added to the curd, and a second pressure was applied for 12 h at the same weight as the milk. Chickpea-sized cheese samples were tightly packed in a plastic screw cap box and matured at 4 °C for 120 days. The curd efficiency was calculated as the ratio of curd to milk. The yield percentages for raw, thermized, and pasteurized milk curds were 26.7, 38.6, and 21.1, respectively. Dry matter levels were similar (45% on average) in all three cheeses. Pasteurized milk cheeses achieved acceptable microbiological quality on the first day, thermized milk cheeses on the 60th d, and raw milk cheeses on the 90th d. During the process, raw milk cheeses' pH climbed from 5.4 on the first d to 7.1 on the 120th. These values were measured in pasteurized milk. Pasteurized cow's milk improved acidity and pH to an acceptable level. It was determined that Siirt Herby Tulum Cheese may be made from pasteurized cow's milk, with a minimum of 20% fat, 20% protein, 45% dry matter, and a maximum of 2% salt. The proposed method has the potential to improve manufacturing standards, hygiene, and cost-effectiveness. It is possible to conduct additional research on the subject and build the best industrial manufacturing procedure.

Keywords: Cow's milk, Siirt herby cheese, thermization, pasteurisation, ripening

Çiğ, Termize ve Pastörize İnek Sütünün Siirt Otlu Tulum Peyniri Yapımında Kullanımı

Özet: Bu çalışmada, bir çiftlikten alınan inek sütünün çiğ, termize ve pastörize formları kullanılarak Siirt otlu tulum peyniri üretildi. Üretim ve ambalajlamanın 24 saat içerisinde tamamlanması sağlandı. Süt, 72˚C 1 dk süreyle pastörize edildikten sonra 32 ˚C'de 90 dk süreyle mayalandı. Pıhtı 1x1x1 cm pıhtı büyüklüğünde kırılarak 45 dk bekletildikten sonra 15 dakika süreyle süzüldü. Süzülen telemenin % 1'i kadar tuz eklenen teleme 12 saat süreyle süt ağırlığının yarısı kadar ağırlık altında birinci baskı uygulandı. Teleme kırılarak sirmo (*Allium* sp.) eklendi ve kullanılan sütün ağırlığına eşit ağırlık altında 12 saat süreyle ikinci baskı uygulandı. Nohut büyüklüğünde ufalanan peynir örnekleri plastik vida kapaklı ambalajda 4°C'de 120 gün süre ile olgunlaştırıldı. Pıhtı kırmadan sonra kendiliğinden süzülen teleme miktarının süte oranı kullanılarak teleme randımanı hesaplandı. Çiğ, teremize ve pastörize süt telemelerinde % randıman sırası ile 26,7, 38,6 ve 21,1 olarak tespit edildi. Her üç peynirde de benzer kuru madde düzeyi (ortalama %45) tespit edildi. Pastörize süt peynirlerinin ilk günde, teremize süt peynirlerinin 60. günde ve çiğ süt peynirlerinin 90. günde uygun mikrobiyolojik kaliteye ulaştığı gözlendi. Süreç içerisinde çiğ süt peynirlerinde pH ilk günde 5,4 iken 120. günde 7.1'e yükseldi. Pastörize sütte ise bu değerler 6,1 ve 5,9 olarak ölçüldü. Pastörize inek sütü kullanmakla yeterince asitlik ve pH gelişimi gözlendi. Pastörize inek sütü kullanılarak içeriğinde en az %20 yağ, %20 protein, %45 kuru madde ve en fazla %2 tuz olacak şeklide Siirt otlu tulum peyniri üretiminin yapılabileceği görüldü. Daha standart, hijyenik ve ekonomik üretim yapılması için önerilen metot yararlı olabilir. Konunun daha fazla araştırılması ve ideal endüstriyel üretim prosesinin geliştirilmesi sağlanabilir.

Anahtar Kelimeler: İnek sütü, Siirt otlu peyniri, termizasyon, pastörizasyon, olgunlaştırma.

1. Introduction

Türkiye has 193 cheese kinds, making it one of the countries with the most. Although the basic production processes for these cheeses differ slightly, the resulting product exhibits distinct characteristics (1). Cheese's contribution to tourism can be increased by standardizing its production in Anatolia, ensuring its hygiene, and ripening it (2-4). The proportion of traditional cheeses among the 753 thousand tons of cheese produced in Türkiye is unknown (5). The most common type of herby cheese is Van Herby Cheese, which has a Geographical Indication Certificate (6). Other herby cheeses include Urfa, Bitlis, Hakkari, Trabzon, Erzincan keçene, and Siirt. Siirt Herby Cheese is often made from raw sheep milk or a combination of sheep and goat milk. While sirmo (sirik, *Allium* sp.) is the most common herb added to cheese, it has been noted that herbs such as heliz (*Ferula orientalis*) and

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ciriş (*Eremurus spectabilis*) are also used depending on the consumer's preferences (7).

Scientific research has led to the achievement of industrial production and national consumption of Van Herby Cheese (8–16). For other regional herby cheeses, there was only one available scientific study (17). Official documents specify the minimum technical and hygienic standards for cheeses, and official inspections are conducted in accordance with these standards (18–20). Herby cheeses' chemical and microbiological quality attributes were examined, and any potential health problems were highlighted. It has been demonstrated, therefore, that the sanitary quality and contents of regional cheeses made by non-commercial businesses are subpar (21-33). According to reports, Siirt Herby Cheeses sold at points of sale do not meet norms for chemical and microbiological quality (34–37).

Studies on Van Herby Cheese have indicated that using cow's milk is appropriate (10,11,13, 14). These days, big businesses sell their cow's milk-based Van Herby Cheeses over the country. When it comes to the number of sheep and goats, Siirt is one of the major provinces. But getting enough milk and making enough herby cheese to sell nationwide seems to be a challenge. Thus, in this investigation, pasteurized cow's milk was utilized. This will likely be the first experimental study utilizing pasteurized cow's milk on Siirt Herby Tulum Cheese. We think the results could help in the future to enhance the product's technological production process.

Models of Van Herby Cheese production have been thoroughly examined (8–16). Following the pasteurization of various milks, herby cheeses were vacuum-packed and their chemical alterations were monitored for ninety d. According to reports, there are no appreciable differences in the finished product's qualities when using goat milk either by itself or in conjunction with cow milk (15). Using raw and pasteurized cow, sheep, and goat milk, Tunçtürk et al. (38) created both raw milk cheese using the conventional method and cheese samples using the model industrial production method employing pasteurization and starting culture. They then looked at the changes that occurred over the ripening phase. No recommendations for technological processes were given as a consequence of the investigation. An experimental study on Siirt Herby Cheese used sheep's milk. According to studies, additional study is required before cheese can be sold (17). The development of a technological procedure appropriate for cow's milk could aid in the national production and promotion of Tulum cheese flavored with herbs. Cow's milk was used in this investigation to prepare samples of raw, thermized, and pasteurized milk cheeses, which were then matured for 120 d at +4°C. With the understanding that the samples' physical, chemical, and microbiological characteristics complied with applicable regulations and laws, every attempt was made to manufacture and package the cheese in less than a day.

2. Material and methods

Materials

Raw milk: The milk, which was milked on a farm near Siirt's city center, was filtered with a cloth strainer and sent to the laboratory within an hour, where it was separated into three equal pieces. Portions were utilized to make raw, thermized, and pasteurized milk cheeses. The created cheeses were packed tightly into 100 ml sample containers, leaving no air space. Cheese samples were ripened at +4°C for four months and analysed once a month.

Rennet: Rennet was purchased from a local market, brought to the laboratory and kept at room temperature.

Herb (Sirmo, Sirik, *Allium* sp.): Citizens harvested herbs from the plateaus and sold them in the market. After being sorted and cleaned with drinking water, the herbs were chopped to about 5 mm size and mixed into the curd at a rate of 3% (w/w) between the first and second presses.

Salt: Local rock salt used in cheese production was employed.

Press material: Plastic containers filled with water were used on the curd and curd formed into a bundle in a filter cloth.

Making herb cheese using raw milk: Raw cow milk was heated to 35°C. Calcium chloride (200 ppm, w/v) was mixed into the milk. The rennet was added to the milk at 32°C and left for 90 minutes. The clot was sliced to 1x1x1 cm size and left for 45 min. The clot was placed in a press towel and filtered for 15 min. The resulting curd was crumbled into chickpea-sized pieces and mixed with 1% of the curd's weight in salt. The salted curd was subjected to the initial pressure for 12 h with a weight equal to half that of the milk. The curd was crushed to the size of chickpeas, and 20% of the milk solids were combined with Sirmo (*Allium* sp.). For 12 h, the curd was subjected to a second pressure equal to the weight of the milk. At the end of the pressing, the curd, which had crumbled to the size of chickpeas, was securely packed into plastic containers.

Making herby cheese using thermized milk: Raw sheep milk was therified at 65˚C for 1 minute and immediately cooled to 37˚C. All other processes were applied as in raw milk cheese making.

Making herb cheese using pasteurized milk: To make herby cheese, raw sheep milk was heated to 65˚C for 1 minute before cooling to 37˚C. All other processes were carried out in the same manner as for manufacturing raw milk cheese.

Making herby cheese using pasteurized milk: Raw sheep milk was pasteurized at 72°C for 1 minute and then cooled to 37°C. All other processes were carried out in the same manner as when manufacturing raw milk cheese.

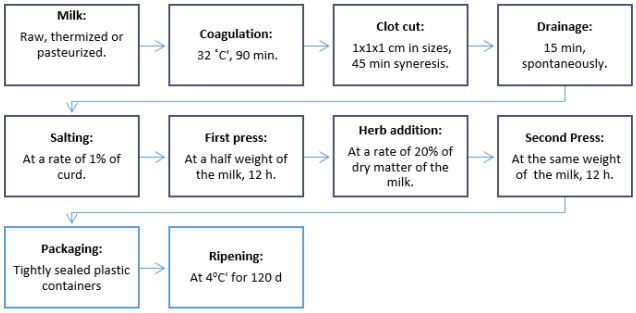


Figure 1: Experimental Siirt Herby Tulum Cheese making.

Raw milk analyses: Raw milk pH was measured using a handheld pH meter (AZ 8685, Taiwan). Acidity was determined using the titrimetric method, and the findings were reported as %LA. Milk was also examined using a milk analyzer (Lactoscan LS, Nova Zagora, Bulgaria) (39).

Coagulant Strength determination: Coagulant strength was determined by diluting the coagulant (Yayla Rennet, Tuzla Istanbul) by one-tenth. Raw milk was heated to 35°C. 1 mL of diluted coagulant was added to 10 mL of hot milk, and the clot formation duration was measured. The coagulant strength was determined using the formula (40).

Analysis of milk, curd and cheese samples

The pH and acidity of the samples were determined according to Sadler and Murphy (39), dry matter was determined gravimetrically according to TS EN ISO 5534/AC (41), fat was determined using the Van Gulik method (TS ISO 3433) (42), and salt was determined gravimetrically according to TS EN ISO 5943;2007 (43).

Microbiological tests were conducted on 10 mL of raw milk and 10 g of cheese. Cheese samples were homogenized by external hand maceration in 90 ml of sterile physiological saline (FTS) in a sterile sample bag. One of the homogenates was employed in serial dilution. The pour plate technique (44) was used to inoculate 1 mL samples from repeated dilution tubes. Coliform group bacteria were counted on solid media using TS ISO 4832 (45), then spreaded onto Violet Red Bile Lactose Agar (VRBLA, Oxoid CM0107). After 24 h of incubation at 30 °C, pink-red colonies with a pink precipitation ring were counted. The coagulase test and counting of Coagulase-positive staphylococci were carried out in accordance with TS EN ISO 6888-1 (46). Baird Parker Agar (BPA) petri plates were utilized, which were then incubated at 37°C for 48 h. The real number was determined by performing a coagulase test on ten black lustrous colonies with a diameter of 1.5 - 2.5 mm and a translucent zone surrounding them.

Statistical analysis

One-way analysis of variance (ANOVA) followed by a Duncan test was done to verify differences between means using IBM SPSS Statistics 28 (IBM Corporation, Somers, NY, USA). Differences were considered significant at the probability level $p < 0.05$.

Results

The raw milk analysis findings are shown in the table. When the analytical values were evaluated, it was found that they were within the cow's milk criteria, with no anomalous values detected. It was found that the fat ratio was 3.29%, the protein ratio was 3.1%, and the density was 1.034. The pH of raw milk was found to be 6.8, and the acidity was 0.18 (%, lactic acid). In raw milk curd, the pH of the strained curd prior to the first pressing is 6.0; in thermized milk curd, it is 6.2, and in pasteurized milk curd, it is 6.8. The three curds' relative acidities were found to be 0.25, 0.21 and 0.18.

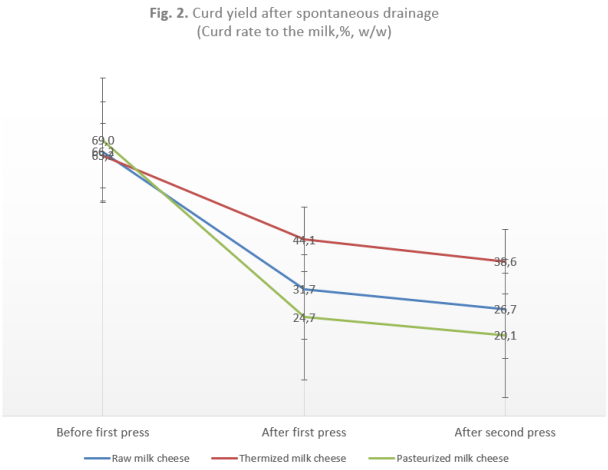
Table 1: Analytical results acquired after 15 minutes of spontaneous draining of the curd formed from cow milk used to make cheese.

	pH	Acidity (lactic a., %)	Dry matter (w/w, %)	Protein (w/w, %)	Yağ (w/w, %)	Laktoz (w/w, %)	Minerals (w/w, %)	Density (w/w, %)	Freezing point(°C)	Conductivity (Ω' cm')
Raw milk	6,9	0,18	13,6	3,25	3,29	4,88	0,74	1,031	-0,566	6,19
Raw milk clot	6,0	0,25	ND*	ND	ND	ND	ND	ND	ND	ND
Thermized milk clot	6,2	0,21	ND	ND	ND	ND	ND	ND	ND	ND
Pasteurized milk clot	6,8	0,18	ND	ND	ND	ND	ND	ND	ND	ND

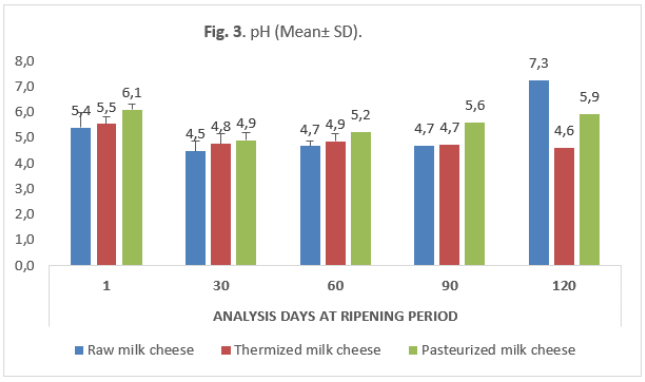
*: Not determined.

The microbiological investigation of raw milk revealed the presence of Coagulase-positive staphylococci at 3.9 log cfu/ml and coliform group bacteria at 6.3 log cfu/ml. Tables and figures have not used to display these results.

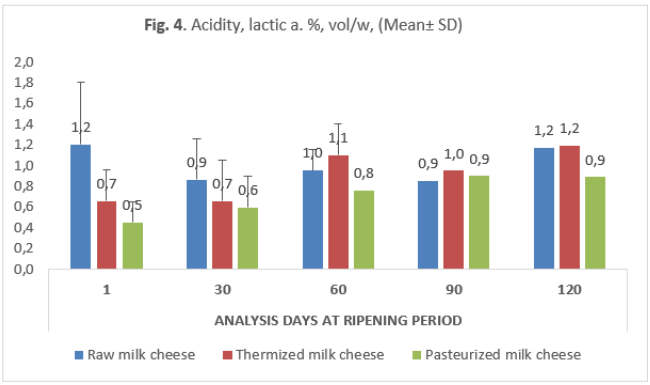
Weights were taken three times after the clot was extracted. The collected values were proportioned to the weight of the milk used to get the efficiency percentage. Following spontaneous filtration, the curd's yield values (%) after the first and second pressings were determined to be as follows: 31.7 and 26.7 for the raw milk cheese samples, 44.1 and 38.6 for the thermized cheese samples, and 24,7 and 20.1 for the pasteurized cheese samples. Figure 2 provides the values.



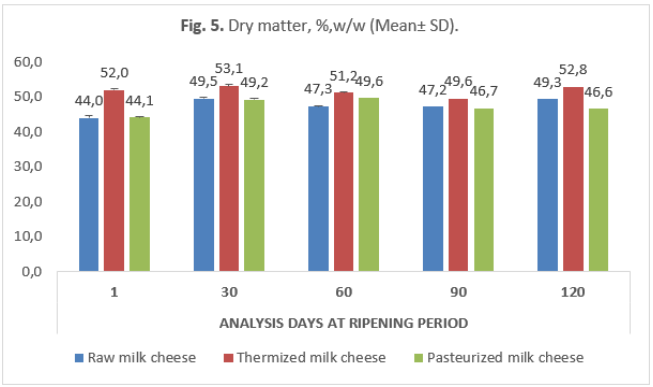
Three distinct cheeses were created by preparing three distinct curds in the same way. The cheeses were then sealed in plastic sample containers with lids and allowed to ripen at 4 °C. Analyses were carried out on ripening d 1, 30, 60, 90, and 120. At every level of the analysis, it was discovered that the pH values that were acquired from the analyses varied. Pasteurized milk cheeses were shown to have a higher pH than other varieties from the first to the ninety-first d. Up to this point, there was a statistically significant difference ($p<0.05$) in the pH values of the two samples. On the other hand, raw milk cheese was found to have an abnormally high pH (7.3) on d 120. The pH of pasteurized milk cheese was found to be 5.9, whereas that of thermized milk cheese is 4.6. In Fig. 3, pH values are displayed.



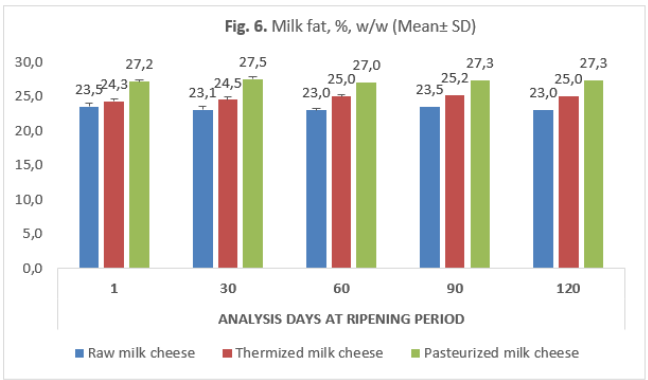
For every d of analysis, distinct acidity values were found for each of the three types of cheese. Every one of these numbers was shown to be statistically distinct from the others. The acidity value of raw milk cheese is 1.2 on the first d it is prepared and packed; for thermized milk cheese and pasteurized milk cheese, it is 0.7 and 0.5, respectively. The acidity of the processed milk cheese rose and the raw milk cheese fell during the next d, approaching one another. The value difference between these two cheeses has dropped to 0.1%, notwithstanding a statistical difference between them. On the 120th d of ripening, the acidity values (1.2) of raw milk and thermized milk cheese were comparable; however, in pasteurized milk cheese, this value was found to be 0.9 (Figure 4).



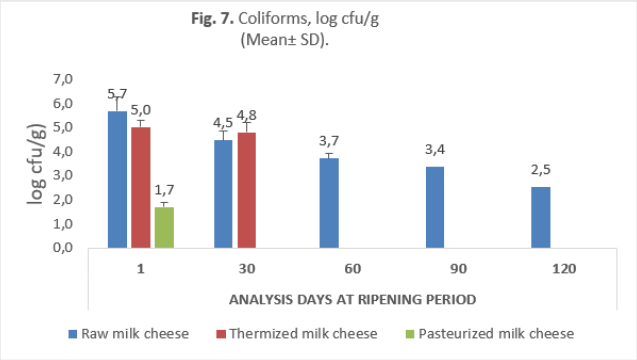
The dry matter levels of the cheeses made from heated milk had the greatest values when ordered from high to low. A statistical confirmation of this difference was also found ($p<0.05$). There was no apparent distinction between pasteurized and raw milk cheese. It was noted that the samples' moisture loss was not appreciably low. Figure 5 provides the values.



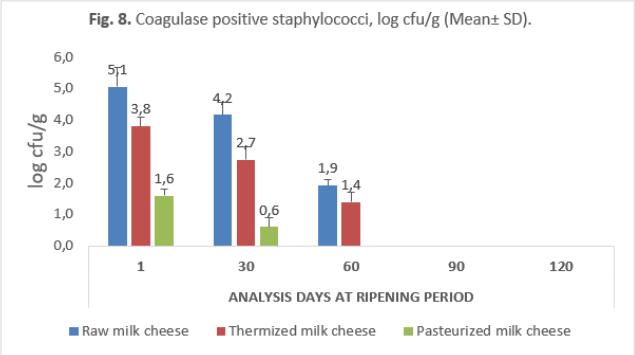
For every d of analysis, distinct fat values were found for each of the three varieties of cheese. Every one of these numbers was shown to be statistically distinct from the others. The cheese's percentage fat value is 23.5 in raw milk cheese on the first d it is prepared and packaged; it is 24.3 in thermized milk cheese and 27.2 in pasteurized milk cheese. There was a statistically significant difference ($p<0.05$) in the fat content of the cheeses. Throughout the ripening phase, the values stayed quite stable (Fig. 6).



In the cheese that was packed, the amount of salt that was added at a rate of 1% of the curd weight prior to the first pressing was measured at 2.05%. The salt levels in its packaging did not alter as it ripened, and these results have not been reported before. The raw milk and fermented milk cheeses were found to contain very high levels of coagulase-positive staphylococcus populations. In raw milk cheese, the degree of contamination was found to be 5.1 log cfu/g, but in therified milk cheese, it was found to be 3.8 log cfu/g. In raw milk, these values were found to be 3.9 log cfu/g (the datum has not been given in Tables or Figures). During the cheese production step, an increase in Coagulase-positive staphylococci was found. Pasteurized milk cheeses had a contamination level of 1.6 log cfu/g, which is acceptable and less than what needed to be counted on the 60th d. In raw milk cheeses, the number declined significantly until the 60th d, however it only dropped to 1.9 log cfu/g. Even on the 60th d, a large quantity of Coagulase-positive staphylococci (4.2 log cfu/g) was found in raw milk cheese. On the 90th d of ripening, it was noted that the amount of coagulase-positive bacteria in all samples dropped below the countable threshold (>10 cfu/g) (Fig. 7).



Both raw milk and fermented milk cheeses have extremely high concentrations of coliform bacteria. In raw milk cheese, the degree of contamination was found to be 5.7 log cfu/g, while in the thermized milk cheese, it was found to be 5.0 log cfu/g. In raw milk, these values were found to be 6.3 log cfu/g. Coagulase-positive staphylococci were found to be more prevalent throughout the cheese production phase. The allowable contamination level in pasteurized milk cheeses was found to be 1.7 log cfu/g, and on the 30th d, it dropped below the countable limit. In raw milk cheeses, the number dropped gradually until the 120th d, although it only dropped to 2.5 log cfu/g. On the 30th d, there were even more Coagulase-positive staphylococci (4.8 log cfu/g); nevertheless, on the 60th d, the amount was seen to fall below the countable level (Fig. 8).



Discussion and Conclusion

Siirt Herby Tulum Cheese is packaged without the use of mold cheese; instead, the cheese is crushed and pushed into the container, unlike other herby cheeses, which employ Cacik (Cacık in Turkish) (17, 37). To get rid of extra salt from the cheese, cheese molds are cleaned in water after being dry salted. After that, the molds are broken apart and imprinted on the package. The likelihood of the cheese becoming tainted rises in this situation. The conventional production method's use of raw milk could be another cause of infection. We think it's difficult to keep cheese from getting contaminated in unsuitable places, like under the stairs or in a home.

There may be variations in the quality of the final product if milk is used in production without consideration for variables like breed, age, race, season, and mixing ratios that affect the content of milk. As a result, before milk is turned into cheese, it must be standardized (23). The technology used to produce Siirt Herby Cheese can be improved by carrying out in-depth research on this topic.

The tissue in herby cheeses breaks up into little lumps either on its own or when pressure is applied. The cheeses have to be completely dried out and seem semi-dry in order to acquire this texture. To achieve this, a large quantity of salt and press weight are employed, and the press time is increased by three to four d. The cheeses are kept at about 20°C during this time to guarantee that the acidity rises and ripening starts (5,6,10,23). We think that extensive manual processing and a prolonged production process are unsuitable for sanitary and modern production. Because of this, we believe that, as was done in this study, it would be suitable to complete the production in a d and package the product the same d. There is no prior research on this topic pertaining to herby tulum cheese that we are aware of. The findings of microbiological and chemical analyses indicate that herby tulum cheese can be made from pasteurized cow's milk in less than a d (Fig. 3–8).

Only the values for moisture, dry matter, fat in dry matter, and salt in dry matter are included in the Herby Cheese Standard (47). Values for dry matter, fat, ash, and salt are included in

the Geographical Indication Certificate (5) for Van Herby Cheese. Values for pH and acidity are absent from both papers. The Herby Cheese Standard does not include an ash value. The pH, acidity, and protein content of cheeses are not covered by the law. This suggests that when developing processes, there is no set norm for acidity and pH.

The table displays the results of the milk and curd analyses. It was found that milk had a density of 1.031, a fat content of 3.29%, and a protein content of 3.1%. It was found that raw milk has a pH of 6.8. The pH of the curd filtered before the first pressing in the samples was found to be 6.0 in the case of raw milk curd, 6.2 in the case of thermized milk curd, and 6.8 in the case of pasteurized milk curd. It has been noted that this is a typical occurrence and that the bacteria found in raw and heated milk both multiply and lower pH levels while cheese is being made. Similar to this, it was found that the acidity of raw milk curd dropped to 0.25% and the acidity of curd milk curd to 0.21%, despite the fact that the acidity of raw milk (lactic acid) was 0.18%. The acidity of pasteurized milk (0.18%) stayed constant with that of raw milk. The same explanation that applies to pH also applies to this circumstance. By eliminating the tainted flora, pasteurization stopped the pH drop and acidity rise. Nonetheless, it is known that curd has a high enough acidity in both raw and heated milk to raise acidity and lower pH during the production stage. This is not the right environment for making cheese the normal, healthful way. Ultimately, we noticed a discernible drop in indicator microorganisms (coagulase positive staphylococci and coliform) in the samples we prepared on the 60th ripening d (Figures 7,8). Similar to raw milk, thermal milk is not ideal for making cheese right away. But more thorough study needs to be done on this topic, including a look into what kind of milk can be used to make cheese after thermization rather than pasteurization. It was believed in this investigation that the high microflora load of milk (3.9 log cfu/ml coagulase positive staphylococcus and 6.3 log cfu/ml coliform) prevented termization from offering adequate assurance. Pasteurized milk cheeses did not exhibit a fall in pH or an increase in acidity. In this instance, using starter culture and/or ripening culture in cheeses ingested after ripening is required, as all scientific research recommend.

According to the Turkish Food Codex Microbiological Criteria Communiqué (19), as a hygienic requirement, the amount of Enterobacteriaceae in pasteurized milk may not exceed 10 log cfu/ml. The rule for pasteurized milk does not include any values for coagulase positive staphylococcus or coliform. Given that the study's raw milk had 6.3 log cfu/ml coliforms and 3.9 log cfu/ml Coagulase-positive staphylococci - both of which were significantly higher than the maximum permitted quantity of *Enterobacteriaceae* (10 log cfu/ml) - it is recognized that raw milk of this quality should not be used to process thermized milk into cheese without pasteurization. It was shown that the samples' bacterial population, including Coagulase-positive staphylococci and coliform, which are regarded as markers, was high even during the ripening period (Figure 7,8). The number of colonies in the milk at 30°C (per ml) must be < 500,000 if raw milk from species other than cows is to be utilized in the making of raw milk cheese without any heat treatment (24). The coliform count (6.3 log cfu/ml) in the milk utilized in this investigation was found to be even higher. It was shown through the examination of cheese samples obtained from sales locations that Siirt Herby Cheeses' hygienic quality did not meet requirements (37). According to Gülmez et al. (17), pasteurized sheep milk is required for the manufacturing of Siirt Herby Tulum Cheese, as raw or matured milk is not acceptable.

Twenty pieces of Siirt herby tulum cheese were measured for pH at a minimum of 4.4 in Siirt province sales points. The highest value measured was 6.3, while the average was 5.3 (37). A different earlier study found that throughout the course of 90 d of ripening, the pH of herby cheese dropped from 4.89 to 4.52 (15). The pH level of the herby cheese samples taken at the sales point has been reported to be at least 4.2, average 5.3, and maximum 6.8, based on the results of numerous other studies (4,7,8,21,28,36). The pH value of 7.3 found in this study's experimentally manufactured raw milk cheese on the 120th d of ripening is noticeably higher than the values found in other research. It is unacceptable for cheese to have this pH level. Thermized milk cheese and pasteurized milk cheese were found to have pH values of 4.6 and 5.9 on the 120th d, respectively (Fig. 3.4). The samples were produced using pasteurized milk, however neither a starting culture nor a ripening culture were utilized. Nonetheless, pH dropped and acidity rose. The bacteria that caused the fermentation were those that survived pasteurization and subsequent contaminations during processing and were spread by herbs, yeast, and/or the indigenous b of milk. Pasteurized milk cheeses were found to have a pH that dropped until the 30th d and then climbed, reaching 5.9 on the 120th d (Fig. 3). It has been previously documented that Siirt Herby Cheeses produced with pasteurized milk had changes in pH and acidity (17). This was taken to mean that the pH was rising and ripening was still ongoing. It was determined that thermized milk cheeses had superior pH stability. Making pasteurized milk cheeses with milk that has starter culture in it is more appropriate (9,13,14, 17). We think it would be good to ascertain the acceptable pH ranges for cheeses, including herby cheeses, that are sold after ripening in their packaging.

The acidity of the herby cheeses marketed in the Siirt city center was found to be at least 0.8 in earlier tests; the highest was found to be 4.1, and the average was 1.9 (37). According to reports from other researchers that examined herby cheeses bought from sales points, several samples had acidity values as low as 0.11% (13), 0.18% (23) and 0.24 (14). These values

are unique to curd cheese, thus it's possible that matured tulum cheese has different causes for them to exist. It could be argued that protein deterioration or overripening neutralize acidity. According to a study, throughout the ripening stage, the acidity (%, lactic acid) increased from 0.62% to 1.05% (15). In a recent study, it was shown that during the 120-d ripening phase, the acidity of Siirt Herby Cheese—which is made with sheep's milk—rose to a level of 0.8% lactic acid. The findings of this investigation showed that on the 120th d, the discrepancies between raw and pasteurized milk cheeses closed and equalized (17). We think that when making Siirt Herby Cheese, it would be advantageous to adjust the acidity to reference standards.

Herby tulum cheeses are produced differently and have similar chemical compositions to other tulum cheeses, but according to the Tulum Cheese Standard (48), their dry matter content must be at least 45% and their moisture content no more than 45% (or 50% in the case of low-fat and fat-free tulum cheeses). The Herby Cheese Standard (47), however, claims a greater moisture value (maximum 60%). The value of this is comparable to that of white cheese. According to Gülmez et al. (17), samples of Siirt Herby Tulum Cheese prepared with sheep's milk had varying levels of dry matter (41–46%). In their examination of samples of herby cheese obtained from sales locations in Siirt's city center, Gülmez et al. (37), discovered that the cheeses' dry matter content was at least 34.6%; they recorded a maximum of 57.9% and an average of 49.6%. There are significant variations in the dry matter ratios of the cheeses that are sold, according to research. It was noted in other earlier research that the dry matter ratio of the Siirt Herby Cheeses sold was not typical (34–36). According to reports, the dry matter content of the cheeses sold at Bitlis, Hakkari, and Van Herby Cheeses varies significantly (21-28,29,30, 32). Cheeses packed in airtight packaging have very little moisture loss (8,12,14, 17). Despite using cow's milk in this investigation, the cheeses' dry matter content was only about 50% (Fig. 5). This data leads us to assume that, similar to other tulum cheeses, it would be OK to market herby cheeses with a dry matter standard of at least 45% and ideally at least 50%.

The percentage of milk fat in dry matter is stated to be at least 45% in the Herby Cheese Standard (47), at least 16.75 percent at most 19.21 percent, and on average 17.29 percent in the Van Herby Cheese Geographical Indication Certificate (5). According to Gülmez et al. (17), samples of Siirt Herby Tulum Cheese prepared with sheep's milk had an average fat content of 18%. In their examination of herby cheese samples obtained from sales locations in Siirt's city center, Gülmez et reported similar outcomes. It was noted in raw, pasteurized, and thermized sheep's milk milk cheeses in an earlier experimental investigation by et al., and it was stated that only pasteurization could offer adequate sanitary guarantee. In their examination of twenty samples of herby cheese obtained al. (37) discovered that the cheeses' dry matter included a minimum of 31.2% fat; the highest percentage they recorded was 63.5%, and the average was 46.8%. It was noted in other earlier research that the dry matter ratio of the Siirt Herby Cheeses sold was not typical (34–36). The dry matter contents of the cheeses sold at Bitlis, Hakkari, and Van Herby Cheeses have reportedly been shown to differ significantly (21–28,29,30, 32). It has been noted that there can be a 20–30% variation in fat content amongst cheeses that are sold (37). According to these research, the dry matter ratios of the cheeses that were for sale varied significantly. We think it would be fair to set a minimum and maximum fat level of 20% and 25% for herby cheeses. We found that Siirt Herby Tulum Cheese made using cow's milk can have fat values that are standardized between 20 and 25 percent in this experimental study (Fig. 6).

The maximum permitted salt concentration in the dry matter of tulum cheese according to the Cheese Communiqué (20) is 5%. It is acknowledged that Tulum cheese should have a maximum salinity of 2.25%. According to the Herby Cheese Standard (47), the maximum salt content is 7.5%, whereas the Van Herby Cheese Geographic Indication document states the maximum salt content is 6.9%. They discovered that the dry matter of the cheeses had a minimum of 1.1% salt content, with a maximum of 4.5% and an average of 2.9%, after analyzing samples of herby cheese that were purchased from Siirt city center sales points (37).

Coagulase-positive staphylococci are the indicator microbe group that must be found in tulum cheese in numerical numbers, with a maximum level of 103 cfu/g permitted, according to the Turkish Food Codex Microbiological Criteria Communiqué (19). According to reports, three of the five samples that were collected for examination should include no more than 102 cfu/g of Coagulase-positive staphylococci, and the other two samples should contain no more than 103 cfu/g. In raw milk, coagulase-positive staphylococcus levels of 3.9 log cfu/g were found. In thermized milk cheese, contamination was found at 3.8 log cfu/g and 5.1 log cfu/g. Coagulase-positive staphylococci were found to be more prevalent throughout the cheese production phase. Pasteurized milk cheeses had a 1.6 log cfu/g contamination level, and their hygienic quality was found to be adequate. On the 60th d in thermized cheese samples and the 90th d in raw milk cheese samples, it did, however, drop to a level that would be deemed hygienic. Other types of cheese were found to drop below the countable level only on the sixty-first d (Fig. 7). Gülmez et al. (17)

from sales locations in Siirt's city center, Gülmez et al. (37) discovered that the cheeses had a minimum of 3.2 log cfu/g, a maximum of 7.3 log cfu/g, and an average of 5 log cfu/g of Coagulase-positive staphylococci. These numbers are all above the level for contamination. High amounts of

contamination were found in samples obtained from sales locations in a few other earlier investigations (21–23,31,35,36).

The Turkish Food Codex Microbiological Criteria Communiqué (19) states that the criterion does not include counting coliform bacteria in cheese. Nevertheless, in order to assess the degree of hygiene and provide specific commentary on the impact of pasteurization and thermization on hygiene, analysis of coliforms was also carried out in this investigation. In raw milk, levels of the coliforms were found to be 6.3 log cfu/g. In raw milk cheese, the degree of contamination was found to be 5.7 log cfu/g and in thermized milk cheese, 5.0 log cfu/g, respectively, exceeding acceptable limits. With the exception of the pasteurized milk cheeses, large levels of contamination (>3 log cfu/g) were found in the other two cheeses on the first d of ripening; however, contamination over this level was only seen in the raw milk cheese at d thirty (Fig. 7). In a prior experimental work with sheep milk, Gülmez et al. (17) found that on the 120th d of ripening in raw milk cheese and on the 90th d of ripening in thermized milk cheese, it dropped below 3 log cfu/g. It has been stated that pasteurization is required to guarantee hygiene. The coliform level in the 20 herby cheese samples that Gülmez et al. (37), analyzed from sales points in the Siirt city center, was found to be at least 1 log cfu/g, at most 9 log cfu/g, and on average 4.6 log cfu/g. These numbers are all above the level for contamination. High levels of contamination, greater than 3 log cfu/g, were seen in samples obtained from sales locations in a few other earlier studies (21-23,31,35, 36).

Because of this, it appears that pasteurized milk must be used in production rather than raw or termized milk, as the existing state of raw milk hygiene is insufficient. Siirt Herby Cheese appears to be able to be made with cow's milk. Cheeses that are low-fat, semi-fat, and full-fat can be made by standardizing the milk that is used. comprehensive analyses of the HACCP system, the industrial production model, the prerequisites, the minimum conditions, a thorough product description, the workflow diagram, the facility layout and operation process, the critical control points, the critical limits, the barrier technology, and the Siirt Herby Cheese recall procedures. It's still not finished. Being one of the initial investigations on tulum cheese with Siirt herb, this study is anticipated to be a valuable resource for future research. We think it would be advantageous to carry out additional research on the topic and create procedures that abide by legal requirements and technical advancements.

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Conflict of Interest

The authors declare no conflict of interest.

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Quality Characteristics of Raw Milk Samples Purchased from Automatic Milk Vending Machines in Nigde Province

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Abstract: This study aims to examine some physical, chemical and microbiological properties of a total of 40 raw milk samples sold in automatic vending machines and unpackaged, by egulations in Niğde province, and to compare the milk samples according to the retailer from which they were purchased. The study also aimed to quantitatively determine carbonate and hydrogen peroxide residues in milk samples and the presence of beta-lactam and tetracycline group antibiotics with a commercial kit. The average value of lactic acid (%) density, fat, protein, non-fat dry matter, lactose, freezing point, and pH values of the samples were determined as 0.153% ± (0.022); 1.028± (0.03) g/ml; 3.525%± (0.656); 3.5%± (0.107); 9% 4± (0.277); 5.134± (0.152); -0.549°C ± (0.018) and 6.55 ± (0.102) respectively. As a result of microbiological analysis of milk, the average number of total aerobic mesophilic organisms, coliforms, fecal coliforms, yeast-molds and micrococci-staphylococci was determined as 5.38 ± (0.47); 3.73 ± (1.11); 2.76 ± (1.66); 2.33 ± (1.86) and 4.29± (1.20) log cfu/ml respectively. Sodium carbonate, hydrogen peroxide, beta-lactam, and tetracycline antibiotic residues could not be detected in the milk samples. The fact that some of the results obtained in the study were found to be outside the limits specified in the codexes and different from the study average reveals that these samples may cause public health problems, especially in terms of microbial quality, and therefore the milk sold in street milk retailers should be analyzed regularly.

Keywords: Milk vending machine, Niğde, raw milk quality

Niğde İlinde Otomatik Süt Satış Makinelerinden Satın Alınan Çiğ Süt Örneklerinin Kalite Özellikleri

Özet: Bu çalışma Niğde ilinde yönetmeliğe uygun olarak, otomatik satış makinelerinde ve ambalajsız olarak satılan toplam 40 çiğ süt örneğinin bazı fiziksel, kimyasal ve mikrobiyolojik özelliklerinin incelenmesini ve süt örneklerini satın alındığı perakendeciye göre karşılaştırılmasını amaçlamaktadır. Çalışmada ayrıca süt örneklerinde karbonat ve hidrojen peroksit kalıntıları kantitatif olarak, beta-laktam ve tetrasiklin grubu antibiyotiklerin varlığının ticari kit ile belirlenmesi hedeflenmiştir. Çalışma sonunda örneklerin laktik asit (%), yoğunluk, yağ, protein, yağsız kuru madde, laktoz, donma noktası ve pH değerleri sırasıyla ortalama olarak %0.153 ± (0,022); 1.028± (0,03) g/ml; % 3.525± (0,656); %3.5± (0,107); % 9.4± (0,277); 5.134± (0,152); -0.549°C ± (0,018) ve 6.55 ± (0,102) olarak belirlendi. Sütlerin mikrobiyolojik analizleri sonucu, toplam aerobik mezofilik genel canlı, koliform, fekal koliform, maya-küf ve mikrokok-stafilokok sayısı sırasıyla ortalama 5.38 ± (0,47); 3.73 ± (1,11); 2.76 ± (1,66); 2.33 ± (1,86); 4.29± (1,20) log kob/ml olarak tespit edildi. Süt örneklerinde karbonat, hidrojen peroksit ve beta-laktam ile tetrasiklin antibiyotik kalıntısı tespit edilemedi. Çalışmada elde edilen bazı sonuçların kodekslerde belirlenen limitlerin dışında ve çalışma ortalamasından farklı bulunması, bu örneklerin özellikle mikrobiyal kalite yönünden halk sağlığı sorunlarına yol açabileceğini dolayısıyla sokak sütü satan perakendecilerde satılan sütün düzenli olarak analiz edilmesi gerektiğini ortaya koymaktadır.

Anahtar Kelimeler: Çiğ süt kalitesi, Niğde, otomatik süt satış makinesi

1.Introduction

Milk, consumed by consumers for both its organoleptic properties and positive effects on health, is an important component of nutrition all over the world, but it is also a suitable environment for the proliferation of many microorganisms, including pathogens (1). In order to adequately ensure its positive effects in nutrition, the physical, chemical and microbiological properties of milk must be of good quality and these properties must be preserved during the sales process. The quality criteria of milk are determined by standard organizations Türkiye and around the world. According to these criteria, raw milk must be provided from herds officially free of brucellosis and tuberculosis, and the milk must not contain pathogenic microorganisms, toxic chemicals and physical contaminants such as antibiotics and preservatives, and must have a normal

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chemical composition, good aroma and high microbial quality (2-5).

Raw milk, sold by small businesses (grocery stores and small markets) under the name of street milk in Türkiye, is consumed by many consumers considering it to be healthy. Various survey studies conducted on milk consumption habits in Türkiye reveal that consumers prefer street milk to other types of drinking milk (Pasteurized or UHT) depending on their socio-economic status. Among the reasons why consumers prefer street milk, they think that this product is healthier and more nutritious and does not contain preservatives (6, 7).

In the Turkish Food Codex Communiqué (TFCC) on the Supply of Raw Milk (4), raw milk is defined as "milk secreted from the mammary glands of farm animals, which has not been heated above 40 ºC or has not undergone any treatment with an equivalent effect". In the same communiqué, it is stated that the temperature of raw milk should not exceed 4°C during sale, and that under these conditions, milk sales must be made through an automatic vending machine made of corrosion-resistant material, which has a temperature sensor and can be easily cleaned. The criteria specified in the communiqué in question control retail milk sales in order to preserve the quality characteristics of raw milk and ensure that the consumer has access to healthy milk. However, considering that raw milk production is generally carried out by small family businesses (8), this study was designed with the idea that the milk collected from the producer and delivered to the sales place and then put into automatic machines may show different quality characteristics depending on the milking and transportation conditions. In the literature review, it is revealed that the storage and sales conditions of the samples examined in studies investigating the quality characteristics of street milk samples in Türkiye are different from each other (9-12). The aim of this study was to determine the physico-chemical and microbial quality of raw milk samples taken from automatic milk vending machines of different retailers in Niğde province, to investigate the presence of preservatives and antibiotics, and to compare retailers in terms of these characteristics.

2. Materials and Methods

2.1. Materials

In this study, a sample was made from retailers selling unpackaged raw milk from automatic vending machines defined in article 10 of the 4th section of the TFCC on the Supply of Raw Milk (4) in the province of Niğde. Between September and November 2023, 5 retailers selling milk through automatic machines were visited in 10-day periods and a total of 40 milk samples were purchased, 8 from each. Milk samples were delivered to the laboratory within two hours via cold chain and analyzed.

2.2. Methods

2.2.1. Physico-chemical Analysis

In order to determine the physico-chemical properties of milk samples, pH measurement (Isolab, 422522), density determination with lactodensimeter, titratable acidity in % lactic acid (LA) (31), fat, protein, lactose, non-fat dry matter (NFD) and freezing point (FP) (Funke Gerber Lactostar 3510, Germany) values were determined.

2.2.2. Antibiotic Residue and Inhibitory Substances Analysis

A commercial kit (Kwinbon Biotechnology, KB02154Y) was used to detect beta-lactam and tetracycline group antibiotics. Drug detection sensitivity in the commercial kit for beta-lactam antibiotics were reported as 2 µg/L, 3 µg/L, 4 µg/L, 6 µg/L, 20 µg/L, 20 µg/L, 40 µg/L, 50 µg/L, 90 µg/L, 10 µg/L for benzyl penicillin, ampicillin, amoxicillin, oxacillin, nafcillin, cefquinom, cefetrizole, ceftriaxone, ceftiofur, cephalonium, respectively. Drug detection sensitivity in the commercial kit for tetracycline antibiotics were reported as 80 µg/L for tetracycline, terramycin, fortimycin, duomycin. The presence of sodium carbonate and hydrogen peroxide in raw milk samples was determined according to Tekinşen et al (13).

2.3. Microbiological Analysis

Raw milk samples (10 mL) were taken and homogenized in 90 mL of ¼ Ringer's solution, and serial dilutions up to 10-5 were prepared with Ringer's solution. All prepapered dilution (1 mL) was used for total aerobic mesophilic organisms, coliforms and fecal coliforms, yeast-moulds and micrococci-staphylococci, respectively. To determine total aerobic mesophilic bacteria (TAMB) counts, petri dishes containing Plate Count Agar (PCA, Merck, Germany) were incubated for 48-72 hours in an aerobic environment at 30 °C, according to the ISO 4833 (14) technique. Violet Red Bile Agar (VRBL, Merck, Germany) was used to count coliform and fecal coliform bacteria and the petri dishes were incubated at 35°C for 24-48 hours for coliforms and 24-45 ºC for fecal coliforms according to ISO 4832 (15). -Incubated for 48 hours. For yeast-mold enumeration, petri dishes containing pH 3.5 Potato Dextrose Agar (PDA, Merck, Germany) with 10% tartaric acid added were incubated at 28°C for 5 days (16). For micrococcus-Staphylococcus counting, after 24-48 hours of incubation at 37°C in Mannitol Salt Phenol-Red Agar (MSA Merck Germany), yellow colonies with a yellow zone around them were counted, and pink and red colonies were counted as staphylococci and micrococci (17). The number of colonies was calculated logarithmically, quantitatively the colony count of samples < 1 log cfu/mL below the limit of detection was set to $\log_{10}$.

2.4. Statistical analyzes

Statistical differences in the physicochemical and microbiological properties of street milk samples on a retailer basis were tested by analysis of variance, and Tukey, Welch and Man-Whitney U tests were applied according to normality distribution. For each group, the normality of the distribution was examined with the Shapiro-Wilk test and the homogeneity of variances was examined with the Levene Test. One Way Anova test was used for group comparisons. The mean results were given with standard deviation. Statistical analyzes were performed using the IMB SPSS®v.24.Ink (SPSS, 2016) package program. P <0.05 and P <0.005 values were considered statistically significant.

3. Results

The milk samples examined in this study was determined as % LA values ranged from 0.081-0.207, with an average of average 0.137 ± (0.026); pH values ranged from 6.24 to 6.69, with an average of 6.55 ± (0.102); % fat ratio between 1.850-5.24, with an average of 3.525± (0.656); % protein between 3.3-3.8 with an average of 3.5± (0.107); % lactose between 4.81-5.44, with an average of 5.133.5± (0.152); density 1.022 -1.035 g/ml, with an average of 1.028± (0.03) g/mL; %NFD ranged from 8.9 to 10.0, with an average of 9.4± (0.277); FP -0.584°C –(-0.510°C) with an average of -0.549°C ± (0.018). It was found that there was a significant difference in terms of % protein value in retailers C and E (p<0.005) (Table 1).

Table 1: Some physicochemical properties of raw milk samples

Physicochemical Properties	Retailers	N	Min.	Max.	Mean± (SD)*
pH	A	8	6.49	6.68	6.578± (0.074)
	B	8	6.43	6.64	6.534± (0.086)
	C	8	6.45	6.63	6.58± (0.058)
	D	8	6.24	6.69	6.533± (0.185)
	E	8	6.46	6.62	6.545± (0.067)
% Lactic acid	A	8	0.117	0.158	0.136± (0.016)
	B	8	0.081	0.176	0.139± (0.034)
	C	8	0.090	0.153	0.124± (0.022)
	D	8	0.081	0.171	0.135± (0.027)
	E	8	0.126	0.207	0.149± (0.026)
Density	A	8	1.022	1.029	1.026± (0.003)
	B	8	1.027	1.031	1.029± (0.001)
	C	8	1.026	1.035	1.029± (0.003)
	D	8	1.025	1.035	1.030± (0.004)
	E	8	1.026	1.035	1.029± (0.003)
Freezing point	A	8	-0.560	-0.513	-0.537± (0.016)
	B	8	-0.566	-0.545	-0.558± (0.007)
	C	8	-0.584	-0.510	-0.537± (0.023)
	D	8	-0.560	-0.539	-0.547± (0.007)
	E	8	-0.580	-0.550	-0.566± (0.01)
% Non-fat dry matter	A	8	8.85	9.76	9.298± (0.309)
	B	8	9.39	9.75	9.563± (0.117)
	C	8	8.92	10.01	9.259± (0.344)
	D	8	9.26	9.60	9.389± (0.119)
	E	8	9.47	9.93	9.701± (0.167)
% Fat	A	8	2.170	5.24	3.930± (1.042)
	B	8	3.250	3.850	3.508± (0.209)
	C	8	1.850	4.170	3.139± (0.818)
	D	8	2.990	3.600	3.336± (0.222)
	E	8	3.380	4.210	3.713± (0.331)
% Protein	A	8	3.32	3.67	3.499± (0.119)
	B	8	3.52	3.66	3.591± (0.044)
	C[1]	8	3.33	3.76	3.474± (0.134)
	D	8	3.48	3.57	3.525± (0.046)
	E[1]	8	3.56	3.74	3.646± (0.066)
% Lactose	A	8	4.82	5.31	5.05± (0.169)
	B	8	5.11	5.30	5.2± (0.062)
	C	8	4.81	5.44	5.033± (0.190)
	D	8	5.03	5.18	5.113± (0.069)
	E	8	5.15	5.40	5.275± (0.089)

*SD: Standard deviation

[1] C and E There is a statistically significant difference. P <0,05 and p<0.005, statistically significant difference in the physico-chemical properties of raw milk samples

The number of TAMB at 30 °C ranged from 4.85 to 6.77 log cfu/ml, with an average of 5.38 log cfu/ml± (0.47); coliform count ranged from 0 to 4.74 log cfu/ml, with an average of 3.73 log cfu/ml± (1.11); fecal coliform count ranged from 0 to 4.74 log cfu/ml, with an average of 2.76 log cfu/ml± (1.66); yeast-mold count ranged from 0 to 4.84 log cfu/ml, with an average of 2.33 log cfu/ml± (1.86); micrococci-staphylococci count ranged from 0 to 5.91 log cfu/ml, with an average of 4.29 log cfu/ml ± (1.20) were found (Table 2).

Table 2: Presence of microorganisms in raw milk samples (log_{10} cfu/ml)

Microorganisms	Retailers	N	Min.	Max.	Mean± (SD)*
Total aerobic mesophilic	A	8	4.92	6.00	5.44± (0.29)
	B	8	4.88	6.50	5.66± (0.55)
	C	8	4.87	5.97	5.25± (0.46)
	D	8	4.85	5.75	5.11± (0.31)
	E	8	4.88	6.77	5.48± (0.58)
Micrococcus-Staphylococcus	A	8	3.74	5.89	4.62± (0.65)
	B	8	3.86	5.79	4.58± (0.79)
	C	8	0	5.26	3.35± (2.17)
	D	8	3.26	5.32	4.28± (0.67)
	E	8	3.97	5.91	4.63± (0.64)
Yeast-Mold	A	8	0	3.86	1.78± (1.92)
	B	8	0	4.84	1.90± (2.10)
	C	8	0	4.30	3.38± (1.43)
	D	8	0	4.21	1.85± (2.0)
	E	8	0	4.16	2.74± (1.72)
Coliform	A	8	3.67	4.74	4.29± (0.45)
	B	8	3.74	4.74	4.21± (0.39)
	C	8	2.26	4.54	3.74± (0.90)
	D	8	0	4.16	2.49± (1.69)
	E	8	3.04	4.72	3.92± (0.66)
Fecal Coliform	A	8	2.44	4.65	3.51± (0.64)
	B	8	0	4.74	2.62± (1.78)
	C	8	0	4.74	3.08± (1.6)
	D	8	0	3.70	1.53± (1.71)
	E	8	0	4.68	3.03± (1.93)

*SD: Standard deviation

Residues of sodium carbonate, hydrogen peroxide and beta-lactam and tetracycline antibiotics could not be detected in any of the milk samples.

4. Discussion and Conclusion

The milk samples analyzed in this study were purchased from automatic milk vending machines that have a temperature sensor and keep the milk at a maximum temperature of 4°C. In the literature research, no study was found in Türkiye in which only milk samples taken from automatic milk vending machines were analyzed. In studies conducted with street milk samples in Türkiye, it was determined that milk samples were obtained from grocery stores, markets and supermarkets, local milk delicatessens, milk collection center cooling tanks, milk producers and food bazaars (9, 11, 12, 18, 19). In some studies conducted abroad, unlike this study, milk samples were collected from milk distribution tankers of traditional farms (20); vendors selling milk in pickup trucks and donkey carts (21), or from the producer after milking (22). It is stated that in many European countries, raw milk is sold self-service in automatic milk vending machines. In these countries, there are studies to determine the quality of milk samples offered for sale in automatic milk vending machines in order to reveal the risks that may occur due to the increase in raw milk consumption among consumers (1, 23-26).

4.1. Physico-chemical Analysis

The total acidity of milk consists of natural acidity and developed acidity. The initial acidity in fresh milk is due to the proteins of the milk, especially casein, and the soluble phosphate, colloidal calcium phosphate, bicarbonate and, to a lesser extent, citrate and carbon dioxide in the milk; the developed acidity is due to lactic acid produced by bacteria from lactose in milk (27). Titratable acidity and pH are physical parameters measured to evaluate the freshness of raw milk, its suitability for hygienic standards and heat treatment, and storage conditions (25). According to the TFCC on the Supply of Raw Milk (4), the acidity value in terms of LA should be between 0.135-0.200%. The LA value of the milk samples examined in this study was found to be

between 0.113-0.207%, with an average of 0.153% ± (0.022). The %LA value of 5 of the samples (12.5%) was detected below the range specified by TFC, and the %LA value of 2 (5%) was detected above the range specified by TFC. Unlike this study, in the study conducted in Erzurum, it was reported that the %LA value was between 0.157-0.178 and within the limits specified in the notification (18). There are studies reporting average % LA values in milk samples as between 0.180-0.270 and higher than this study (10, 12, 21). Alan et al. (11) reported the %LA value as lower than this study (0.16±0.01). Consistent with the findings in this study, it has been reported in studies conducted in Türkiye that %LA values are outside the lower and upper limits of the TFC criteria (10-12). The low %LA value may be due to the addition of an alkaline preservative to the milk, the milk being milked from mastitis-affected breasts, and the large sample size or dilution in the titration method applied (11, 28). In this study, the average pH value was determined as 6.55 ± (0.102), minimum 6.24 and maximum 6.69. The pH value of cow's milk at room temperature is reported to be between 6.5-6.7. The data obtained in this study show that the pH value of some analyzed milk is below average. In studies conducted in Türkiye and around the world, pH values of raw milk samples are reported to be in the range of 5-7.33. (9, 10-12, 18-20, 22). The pH of milk is affected by factors that affect the composition of milk, such as lactation time and mastitis. While the pH value of colostrum is measured around 6, the pH value of mastitis and post-lactation milk can reach up to 7.5 (29). It is accepted that the high level of lactic acid and low pH level in raw milk are largely caused by microorganism activity. Tremonte et al. (26) stated that the pH value of raw milk at refrigerator temperature decreased from 6.72 to 6.27 in 72 hours due to microorganism proliferation. Similarly, among the 40 raw milk samples examined in the study, samples with pH values lower than the average of this study were detected. The microorganism counts of these samples were also found to be higher than the study average (data not shown).

Density, which is one of the physical properties of milk and an important criterion in determining adulteration, is primarily affected by the amount of fat and other chemical compounds in milk. According to the TFCC on the Supply of Raw Milk (4), the density must be at least 1.028 g/ml. In this study, the density of milk samples was determined to be between 1.022-1.035 g/ml, with an average of 1.028± (0.03) g/ml. The density of 12 (30%) of the milk samples examined in the study was found to be below the limit set by TFC. It has been reported in various studies that the density value in raw cow milk samples was determined to be between 1.015-1.035 g/ml (9, 10-12, 19- 22). In this study, it was observed that the % fat values of 11 of the milk samples whose density values were below the TFC (4) limit were above 3.5. It is stated that there is a negative correlation between milk density and the fat rate of milk, and the fat rate is affected by factors such as the genetic characteristics of the animal, feeding practice, seasonal changes and lactation period (30). In a milk sample analyzed in the study, the density and fat rate were found to be below the limit, and the freezing point value was above the limit. It is thought that water was added to this milk sample.

The chemical composition of raw milk, in addition to being an indicator of the chemical compounds that make up the nutritional value of milk, also affects the processability of milk and the quality of the final products (30). According to the TFCC on the Supply of Raw Milk (4), the fat, protein and non-fat dry matter contents in raw milk should be at least 3.4%, 2.8%, and 8.5% respectively. The % fat content in the milk samples examined in this study was determined to be between 1.850 and 5.24, with an average of 3.525± (0.656). According to the Drinking Milk Communiqué (5), all milks to be offered for sale are based on their fat content: full fat (milk fat ≥3.5 g/100 ml), semi-skimmed (1.8 g>milk fat ≥1.5 g/100 ml), skimmed (milk fat<0.15 g/100 ml). In the study, the fat content of 11 (27.5%) samples was found to be lower than 3.4%. It is stated that the % fat content of raw cow milk is between 1.4-7.59% in studies conducted in Türkiye and various countries (9, 11, 12, 18, 22, 24). In this study, the fat content in 11 milk samples was found to be lower than 3.4%, which shows that the milk sold in automatic milk vending machines does not always comply with the criteria set by the codex in terms of quality characteristics. The amount of milk fat is also used in the pricing of raw milk (4), and selling 11 milk samples with low fat content at the same price as other milk creates a negative situation for the consumer.

The NFD value of the milk samples examined in the study was determined to be between 8.9-10.0%, with an average of 9.4%± (0.277), and all of the samples (100%) were found to be in accordance with the value determined in the notification. Studies have shown that the average NFD value is between 8.18-9.32% (9, 11, 12, 18, 19, 22, 24). The NFD value in raw milk is especially affected by the protein and lactose content of the milk. In the milk samples examined in this study, the % protein ratio was determined between 3.3-3.8, with an average of 3.5± (0.107). All samples (100%) were found to meet the criteria, but a significant difference was found between retailers C and E in terms of protein values. Studies have reported that the average protein ratio is between 2.87-3.83 (9-11, 19, 24). In this study, the % lactose value was determined as 5.134± (0.152) between 4.81-5.44. There is no limit for lactose in TFC (4). It is stated that cow milk contains an average of 4.7% lactose, and the amount of lactose affects the freezing and boiling points of milk and its density. In other studies, it is reported that the lactose value was detected between 3.57-5.27% (9, 22, 24). In the milk samples examined in this study, it is seen that the % NFD and % protein and % lactose values affecting the %NFD value are

in accordance with the general chemical composition of milk according to the criteria specified in TFC and the literature.

Evaluation of the chemical quality of raw milk samples was done by determining adulteration with water added by determining the freezing point of milk. According to TS 1018 (31), the freezing point of raw milk is determined as -0.520°C at most. In this study, the freezing point of milk samples was determined between -0.510 - (-0.584)°C, with an average of -0.549°C ± (0.018). The freezing point values of 3 (7.5%) of the milk samples were found to be higher than the criteria specified in TS 1018 (31). In these 3 samples, fat ratios and NFD were determined as 2.9-8.9%, 1.8-8.9 and 2.1-8.9%, respectively, below the average values determined in this study. Freezing point values were found to be between -0.52-(-0.625) on average in other studies (9, 11, 22, 24). It is stated that adding water changes the composition of milk, reduces its specific gravity and nutritional value, and detecting the increase in freezing point is the most important method for detecting the presence of added water (28).

4.2. Microbiological Analysis

Raw milk is an environment containing a diverse and complex microbial population. Factors such as animal cleanliness, milking equipment, conditions of the milking environment, post-milking holding and cold chain affect the microbiological quality of milk. TAMB is one of the important parameters of milk hygiene and is a good indicator for monitoring the hygiene conditions during the production and processing of dairy products. It is reported that the most important factors affecting the microbial behavior of raw milk in terms of TAMB are storage temperature and duration (25). According to the TFCC on the Supply of Raw Milk (4), the number of colonies per milliliter at 30 °C is stated as ≤ 100.000 (5 log cfu/ml). In this study, it was found that 29 milk samples (72.5%) did not meet the specified criteria. Mean TAMB count was 5.38 log cfu/ml ± (0.47); The minimum was determined as 4.85 log cfu /ml and the maximum was 6.77 log cfu /ml. Ertem and Çakmakçı (18) reported that the temperature of raw milk collected from various sales points at the time of purchase was between 9.5-19.0 °C, and the TAMB number varied between 6.17-8.40 log cfu/ml. Also, in various studies where it was not reported that any cooler was used to keep milk cold until sale, the average TAMB number was found to be between 6.93 and 7.36 log cfu/ml (10, 11). However, Açık and Özdemir (9) reported the TAMB number in the milk obtained from cooler tanks in December as 6.74 log cfu/ml, higher than the result obtained in our study. It is stated that in raw milk samples taken from automatic milk vending machines in Europe, this number was found to be between 4.24-4.9 on average, higher than the current study (23, 24, 25). Tremonte et al. (26), similar to this study, reported that the average TAMB count was determined to be approximately 5 log cfu/ml and above the criterion in 10 out of 30 samples.

Since coliform group microorganisms are widely found in nature, they can be transmitted to raw milk due to mastitis infection, wet udder milking, dirty milking containers, fecal contamination and environmental pollution. The presence of high numbers of coliforms in raw milk tanks is considered to be an indicator of improper hygienic condition and inadequate cooling during milk transportation and processing (3, 32). There is no criterion regarding the number of coliforms and fecal coliforms in the dairy and products legislation in Türkiye. In the European Union legislation, it is stated that for general raw milk production, common pathogens should not be detected in defined sample amounts and the coliform count should be <100/ml (2 log cfu/ml) (14). In this study, the coliform count of 37 (92.5%) milk samples was found to be higher than specified in the criteria. The average number of coliforms in the analyzed milk samples was 3.73± (1.11); The minimum was determined as 0 and the maximum was 4.74. The average fecal coliform count was 2.76± (1.66); The minimum was determined as 0 and the maximum was 4.74. The number of coliforms and fecal coliforms has been reported in various studies to range between 1 and 5.50 log cfu/ml, on average, higher and lower than the value we obtained current sudy (12, 18, 19, 26, 33)

It is stated that the psychrotrophic bacteria that multiply during the cold storage of raw milk compete with yeasts and molds in terms of sharing nutrients and limit the development of these microorganisms, thus the number of yeasts and molds should be expected to be low in raw milk obtained under hygienic conditions. Yeast and molds are responsible for spoilage in milk and dairy products, leading to economic losses. It has also been reported that many molds produce mycotoxins that threaten human health (26, 33). In our study, the average yeast-mold count in raw samples was 2.33± (1.86); The minimum was 0 and the maximum was 4.84 log cfu/ml. Yeast-mold counts were reported by Baran and Adıgüzel (12); Alan et al., (10) and Tremonte et al. (26) to average between 4.59, 4.55, and 5 log cfu/ml, respectively.

Micrococci and staphylococci are commonly found in the skin and mucosa of warm-blooded animals, and some species can be used as indicators of microbiological quality (35). In our study, the average micrococcus-staphylococcus count was 4.29± (1.20); The minimum was 0 and the maximum was 5.91 log cfu/ml. The number of micrococci-staphylococci was determined by Tasci (19), Baran and Adıgüzel (12), Alan et al. (11) as an average of 4.32 log cfu/ml; 4.38 log cfu/ml; 2.88 log cfu/ml respectively. Some types of staphylococcus are the causative agent of mastitis, and milk with mastitis is of low physico-chemical quality. Some staphylococcal species pose health risks when presenting raw milk to consumers with the thermostable toxins (36). It is stated that, in addition to mastitis, contamination from the milker and poor care lead to the high number of staphylococci in milk (35).

Although storage in refrigerated machines has been reported as an effective method to keep the microbial load of raw milk under control, in a study, the number of TAMB, coliform, fecal coliform and yeast in raw milk samples kept at refrigerator temperature was 10-25% after 24 hours; It is reported that it increases by 20-50% after 48 hours (26). In the Communiqué on the Supply of Raw Milk, it is stated that the supply of raw milk to the final consumer must be carried out within 24 hours after milking, that the first milking time will be taken as basis for raw milk with different milking times and that the last consumption time of raw milk cannot exceed 48 hours from the first milking time. The numbers of all microorganism groups detected in our study were lower than the

samples obtained from markets, delicatessens, food bazaar etc., but not kept in a cooler (10, 12, 18, 19). However, Açık and Özdemir (9), who obtained raw milk samples from cooling tanks, reported the number of TAMB (average of 5.5×10^6 cfu/mL) and Beykaya et al. (33) reported the number of TAMB (average of $1.48x10^7$ cfu/mL) and yeast mold (average of $3.73x10^5$ cfu/mL) to be higher than the values obtained in this study. This variability in values may be caused by factors such as animal milking hygiene, the time and temperature in which the milk is kept after milking, and the tools and equipment contacted after milking. Milk can be contaminated at different levels with many different microorganism groups in its environment. In addition, in our study, although it was lower than the literature, the TAMB result obtained from the milk of each company was above the limits given in the notification. This situation revealed that the milk initially had a hygiene quality problem and that it was important to be careful against conditions that would increase the number of microorganisms until it was transferred to the vending machine. Coolers will only help ensure that milk reaches consumers in good condition if its microbiological quality is initially high.

4.3. Antibiotic Residue and Inhibitory Substances

No beta-lactam or tetracycline antibiotic residues were detected in any of the raw milk samples. Unlike this study, Ertem and Çakmakçı (18) and Mortaş et al. (37) reported that they found beta-lactam and tetracycline group antibiotic residues in 6.7% and 30%, respectively. Some antibiotics used in veterinary medicine pass to the consumer through milk. It has been reported that various problems occur especially in the quality of fermented dairy products when milk containing antibiotics is presented to consumers, and health risks such as various toxic effects and antibiotic resistance occur in consumers (38).

No traces of sodium carbonate or hydrogen peroxide were found in any of the raw milk samples analyzed. Ertem and Çakmakçı (18); Alan et al. (11) stated that sodium carbonate was added to 66.7% and 20% of the milk they analyzed, respectively. Baran and Adıgüzel (15) and Açık and Özdemir (9) also stated that they could not find carbonate in any of the milk samples they analyzed in Erzurum. Alan et al. (11) also stated that there was no hydrogen peroxide in the milk samples they examined, as in this study. In the TFCC on the Supply of Raw Milk, it is stated that it will not contain any substance other than the component of milk. Despite food legislation, additives such as sodium carbonate and hydrogen peroxide are often used to mask the pH and acidity values of milk that has not been stored properly. It is reported that these additives are harmful to human health, and if consumed continuously, carbonates, for example, cause gastrointestinal problems such as stomach ulcers, diarrhea, and colon ulcers (39).

Although it was determined that the %NFD, %protein and %lactose rates in the street milk samples examined in this study met the criteria and that the samples did not contain carbonate, H2O2 and antibiotics, it was revealed that they did not comply with the regulations in terms of other criteria. According to the results of this study, it was revealed that some of the street milk samples sold in Niğde province were insufficient to meet the targeted health effects of milk consumption and that there were quality differences in terms of physico-chemical and microbiological properties. This study can be used as a basis for future scientific studies as it is the first study to determine the quality characteristics of milk samples offered for sale in accordance with the codex in Turkey. In addition, the low microbial quality determined in some raw milk samples analyzed in the study shows that these milk samples pose a risk to consumer health, even if they are offered for sale in accordance with the codex. In this context, it was concluded that retailers selling street milk should be analyzed regularly in order to check the compliance of the milk samples offered for sale in automatic milk vending machines with the regulations.

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Clinical Efficacy of Bleomycin in Suspected Canine Papillomatosis: Case Report of Two Sibling Puppies

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Abstract: The objective of this case report was to assess the clinical efficacy of anti-tumoral bleomycin on canine papillomatosis (CP) in two male Pug breed sibling puppies. Two 8-month-old, male sibling puppies were presented with multiple warts in the lip and chin. A suspected diagnosis of CP was established through only clinical examination with appearance of typical cauliflower-like warts. Bleomycin was subcutaneously administered to both siblings on a weekly by 0.5 IU/kg dosage. At week 6, one of the siblings exhibited complete regression of oral lesions, whereas the other sibling achieved complete healing by week 9. The warts healed completely, permanently, without new lesions. No adverse effects were observed, verified through weekly blood count and physical examination during and post-treatment. Subcutaneous administration of bleomycin at weekly dose of 0.5 IU/kg contributed to the regression of oral lesions and improved clinical outcomes in dogs, suggesting potential efficiency in the treatment of CP.

Keywords: Bleomycin, Oral lesion, Papilloma, Warts.

Şüpheli Canine Papillamatoziste Bleomisinin Klinik Etkinliği: İki Yavru Kardeş Köpeğin Olgu Sunumu

Özet: Bu olgu sunumu ile anti-tümoral bleomisinin iki erkek, Pug ırkı yavru kardeş köpekte canine papillamatozis (CP) üzerine klinik etkinliğinin değerlendirilmesi amaçlandı. İki 8 aylık yaşta, erkek yavru kardeş köpek ağız ve çene bölgesinde birden fazla siğil lezyonu ile başvuruda bulundu. Şüpheli canine papillamatozis tanısı yalnızca tipik karnıbahar benzeri siğil görüntüsünü içeren klinik bulgular ile konuldu. Her iki kardeşte bleomisin haftalık 0.5 IU/kg dozda deri altı yolla uygulandı. 6. haftada kardeşlerden birinde oral lezyonlar tamamen kaybolurken diğer kardeşte tam iyileşme 9. haftada sağlandı. Siğiller yeni lezyon olmaksızın kalıcı olarak tamamen iyileşti. Haftalık kan sayımı ve fiziksel muayene bulgularıyla takip yapıldı ve tedavi süresince ve sonrasında hiçbir yan etki görülmedi. Deri altı yolla 0.5 IU/kg dozda haftalık uygulanan bleomisinin köpeklerde oral lezyonların gerilemesine ve klinik sonuçların iyileşmesine katkıda bulunması, CP tedavisinde potansiyel etkinliğini desteklemektedir.

Anahtar Kelimeler: Bleomisin, Oral lezyon, Papilloma, Siğiller

1. Introduction

Papilloma is a benign growth of squamous epithelial tissue that occurs due to an infection with papillomavirus. This virus, a double-stranded DNA virus lacking an envelope, has a predilection for mucous membranes and skin in both humans and animals (1). Currently, there are 24 known types of canine papillomaviruses (CPVs), most of which are linked to both mucosal and skin lesions (2). These papillomaviruses exhibit a preference for various organs, with the majority affecting the skin (3). Over time, CPVs have traditionally related to oral-skin-inverted or pigmented plaque papillomatosis in dogs (2). On rare occasions, these viruses have been associated with the development of oral and skin squamous cell carcinomas, occurring in cases of immune suppression (4). Puppies, elderly dogs, and dogs with impaired immune systems are particularly vulnerable to infection (5).

Oral papillomatosis is frequently not requiring treatment and tends to resolve on its own within a period of 3 to 12 months. However, the rapid development and spread of lesions can be occurred in the vulnerable dogs. In these dogs the risk of infection may occur when these growths become massive or appear in challenging regions with picking, chewing and swallowing (6).

There are numerous therapy modalities for the treatment of canine papillomatosis (CP), but the majority have not undergone adequate evaluation (7). The treatment often involves a comprehensive approach that combines various

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methods including surgery, vaccines, and immunotherapy. Surgical interventions may encompass the use of electrocautery, scalpels, lasers, or cryosurgery (8,9). Immunomodulatory therapy might be explored as an option when the patient's immune system is compromised (10-14). In cases of persistent CP that require additional treatment, either due to medical concerns or the pet owner's aesthetic preferences, excisional biopsy or electrocautery is frequently the preferred course of action.

Intralesional bleomycin has been used to treatment of human papillomatosis with great effectiveness, even at low concentrations. Bleomycin has an anti-neoplastic effect and cause acute necrosis in warts with impairing DNA synthesis (12,15,16). Therefore, the objective of the current study was to assess the clinical efficacy of anti-tumoral bleomycin on CP in two sibling puppies.

2. Case Report

Two sibling puppies, an 8-month-old, male and 4-year-old Mother Pug were presented to the private Veterinarian Clinics with history of multiple warts in the lip and chin. The owner stated that the mother had long-standing these warts which was being tried to cure with different administrations (autologous vaccine, azithromycin and surgical removing) however the lesions never regressed and progressively exacerbated (Figure 1). Similarly, the lesions were first noticed approximately 3–4 weeks prior in sibling puppies and they were firstly represented to the veterinarian clinic. The owner did not accept the histopathological evaluation and treatment, so applied to another private clinic. One month later, the owner returned to the clinic with the puppies and was reported that the mother had been euthanized elsewhere.

Figure 1: The unhealed and severe papillomatosis observed in euthanized mother.

Clinical examinations of both puppies were performed before treatment. One puppy had only three small, separated warts present along the lateral aspect of the right lower lip and the middle line of mandible (Figure 2a), other puppy had more severe and bigger multiple warts on the same location with sibling (Figure 3a). A suspected diagnosis of CP was established through only clinical examination. It is important to mention that, apart from oral lesions, no other dermatological abnormalities were observed in siblings.

Upon obtaining consent from the owner, both siblings were initiated on a weekly subcutaneous administration of 0.5 IU/kg bleomycin (®Bleocin-S - 15mg, Onko Koçsel, Istanbul, Türkiye) diluted with 0.9% NaCl. By the week 4 of treatment, despite a reduction in the size of the lesions, an increase in their number was observed (Figure 2b). However, complete resolution was recorded in the following week (Figure 2c). Subsequently, treatment was discontinued after the sixth application for this sibling.

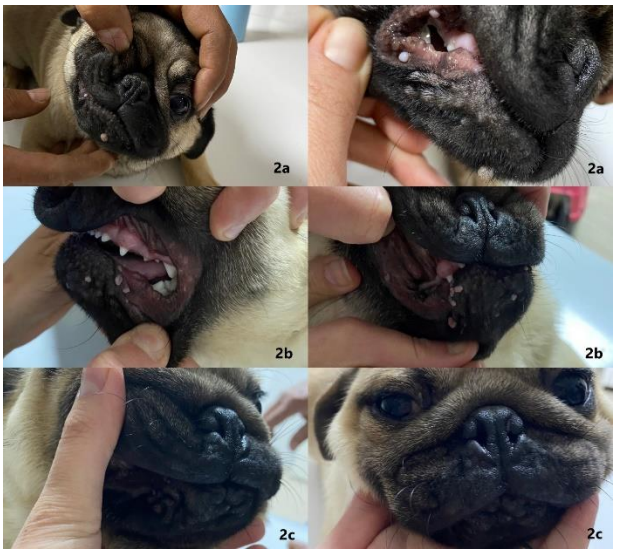

Figure 2: 2a) Varied size of papilloma, small smooth papules present along the lateral aspect of the right lower lip and one cauliflower-like papilloma in the middle line of mandible before treatment, **2b)** Multiple small sized papilloma by the week 4 bleomycin application, **2c)** Complete resolution of lesions by the week 5 of treatment

The other sibling had multiple lesions that persisted for eight weeks without improvement and suddenly complete resolution of the lesions without the reduced size of one wart located in the middle line of the mandible was recorded by the week 9 of bleomycin application (Figure 3b).

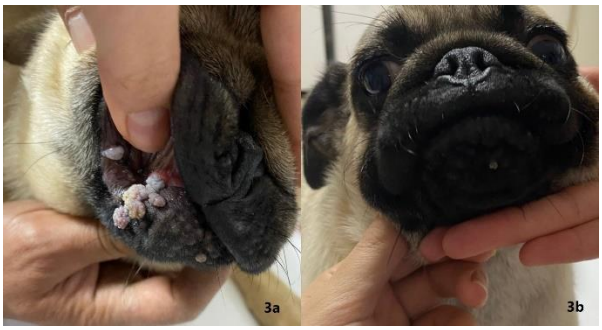

Figure 3: Cauliflower like appearance in the pre-administration of bleomycin (3a) and clinical improvement of

lesions without one more smaller size growth by the week 9 of treatment (3b) in the other sibling

As of 1-year post-treatment the warts continue to exhibit complete resolution, with no evidence of new lesions. No adverse effects were observed throughout the treatment and subsequent follow-up, as confirmed by weekly blood count (Tablo 1) and physical examinations.

Tablo 1: Pre-post treatment blood count of sibling

Parameters	Pre-treatment		Post-treatment
	Case 1	Case 2	Case 1
LYM (10^9/L)	2,8	0,2	1,6
MID (10^9/L)	1,3	0,5	0,8
GRAN (10^9/L)	10,1	9,6	8
RBC (10^{12}/L)	6,49	7,19	6,91
HGB (g/L)	158	171	164
HCT (%)	47,3	51,9	50
MCV (fL)	73	72,2	72,4
MCH (pg)	24,3	23,7	23,7
MCHC (g/L)	334	329	328
RDW-CV (%)	12,5	13,3	12
PLT (10^9/L)	342	474	456
MPV (fL)	8,2	6,8	7,3
PDW (fL)	10,5	8	8,6
PCT (%)	0,28	0,32	0,33

3. Discussion and Conclusion

In this case presentation, both siblings exhibited multiple warts in their lip and chin, clinically consistent with CP. Although spontaneous recovery was observed in these and similar cases, the reason why treatment was applied to the these puppies was the condition of their mothers, to be euthanized due to the severe and chronic process observed despite being exposed to multiple treatments, and the young age of the puppies. However, the owner's reluctance at the referral clinic to undergo histopathological evaluation resulted in a provisional diagnosis of suspected canine oral papillomatosis in these two sibling puppies. Therefore, to assess the clinical efficacy of bleomycin, known for its anti-tumoral activity in human papillomatosis, these two cases were investigated.

Canine oral papillomatosis often resolves spontaneously within 3 to 12 months without requiring treatment, yet susceptible dogs might experience rapid lesion development and spread (6,17). Several surgical and medical approaches are available for treating papillomatosis in dogs, and treatment options may vary depending on the frequency of recurrence, the immunity, and the owner's acceptance of surgical intervention due to aesthetic concerns (8,9). The ideal treatment option aims to eliminate or minimize lesions, preserve skin tissue and integrity, enhance immunity to better combat the disease, and provide lifelong immunity. Numerous therapeutic regimens are considered including the topical application of apple cider vinegar, broad bean wart, vaseline (18), *Thuja occidentalis* (19), imiquimod and 5-fluorouracil (20); oral application of levamisole (21), simethicone (22), alpha interferon (20), human recombinant interferon-alpha 2a (23), *T. occidentalis* (24), acyclovir (25), etretinate (20), azithromycin (10) and homeopathic combination (13); subcutaneous injection of *Tarantula cubensis* extract (26), feline recombinant interferon-omega (27), autogenous vaccine (28) and *T. occidentalis* (29); intramuscular injection of lithium antimony thiomalate (18), *Propionibacterium acnes* (30); intralesional application of alpha interferon (20); intravenous administration of vincristine sulfate, immunoregulin combination (28) and taurolidine (21).

Bleomycin, a cytotoxic agent belonging to the anti-tumor antibiotic subclass and produced from *Streptomyces verticillus* (31), is used in many cancer treatments due to its preferential binding to squamous cells, non-toxic DNA strand breakage/damage (12,33,34). Similarly, it can be administered intralesionally in the treatment of human papillomatosis (12,15,16). Therefore, in the present study, bleomycin was administered subcutaneously once a week in both puppies presented to the clinic with multiple warts on the lip and chin. In one puppy, the lesions were completely resolved after the 5th application, while the other puppy showed improvement after the 9th application. In a meta-analysis encompassing 14 studies involving 2657 patients with common warts (human papilloma), intralesional bleomycin was reported to be more effective than saline or

cryotherapy (32). It's reported that bleomycin on warts induces DNA oxidation by forming metallobleomycin complexes, especially with iron, generating reactive oxygen and causing single-strand and double-strand breaks in DNA between 3'-4' linkages. Furthermore, the activity in tissues is related to bleomycin hydrolase enzyme, also known as cysteine proteinase, and iron content (12).

Pneumonitis and associated pulmonary fibrosis are among the most commonly reported complications of subcutaneous administration of bleomycin in humans and animals (34,35). Gastrointestinal, dermatologic, renal and pulmonary side effects due to high doses of bleomycin have been reported in different experimental studies in dogs (35,36). Pain at the injection site, local swelling and tissue rejection are among the other side effects reported (37). Physical examinations and complete blood analyses were performed weekly on both long-term bleomycin-treated puppies. No symptoms or complications were observed during the treatment period and the following year. A predisposition to pulmonary toxicity has been reported in patients with bleomycin hydrolase deficiency, which detoxifies bleomycin in the lungs (38). It is also stated that high and cumulative doses pose a risk in the development of pulmonary fibrosis (34, 39). In this context, pulmonary side effects have been reported to occur due to the use of doses above 450 IU in adult (40). In the present study, the fact that no side effects were encountered after long-term bleomycin administration in both puppies is consistent with the fact that bleomycin, which is used as part of combined chemotherapy protocols, has lower myelotoxicity than other chemotherapeutic agents (40) and is also reported as a safe agent in combined chemotherapy (41).

In conclusion, in these cases report of suspected CP, subcutaneous administration of bleomycin at a dose of 0.5 IU/kg once a week resulted in regression of oral lesions and clinical improvement.

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Advancing Dairy Cattle Farming: Integrating Herd Management, Automation and Artificial Intelligence for Elevated Productivity and Sustainable Practices

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Abstract: Effective management of dairy cattle herds constitutes a nuanced and intricate process, demanding a blend of technical proficiency, meticulous attention to animal well-being, quality assurance, and continuous monitoring of worker productivity and welfare. The successful execution of these tasks requires a thorough evaluation of diverse data using a well-defined logic, necessitating a professional approach to ensure precise decision-making. The integration of herd management systems, automation, and artificial intelligence applications has become increasingly vital within the realm of dairy farming. These advanced tools are becoming increasingly indispensable and play an important role in guaranteeing the sustainability and profitability of milk production in both the short and long term. From optimizing herd health to streamlining production processes, these innovative technologies contribute significantly to elevating the overall efficiency and sustainability of dairy farming operations. This review aims to examine the evolution and contemporary advantages of herd management systems, automation and artificial intelligence applications in the context of dairy farming.

Keywords: Artificial intelligence, Herd management, Husbandry.

Süt Sığırcılığında İlerleme: Sürü Yönetimi, Otomasyon ve Yapay Zekâ Entegrasyonu ile Artan Verimlilik ve Sürdürülebilir Uygulamalar

Özet: Süt sığırı sürülerinin etkin yönetimi, teknik beceri, hayvan sağlığı ve refahına dikkat, kalite güvencesi ve işçi verimliliği gibi unsurları içeren karmaşık bir süreçtir. Bu görevlerin başarılı bir şekilde yerine getirilmesi, çeşitli verilerin iyi tanımlanmış bir mantık kullanılarak kapsamlı bir şekilde değerlendirilmesini gerektirir ve kesin kararlar alabilmek için profesyonel bir yaklaşımı zorunlu kılar. Sürü yönetim sistemlerinin, otomasyonun ve yapay zekâ uygulamalarının entegrasyonu, süt hayvancılığı sektöründe giderek daha hayati bir rol oynamaktadır. Bu gelişmiş araçlar giderek vazgeçilmez olmakta ve süt üretiminin sürdürülebilirliği ile karlılığını hem kısa hem de uzun vadede garanti altına almada önemli bir rol oynamaktadır. Sürü sağlığını optimize etmekten üretim süreçlerini kolaylaştırmaya kadar, bu yenilikçi teknolojiler süt sığırcılığı operasyonlarının genel verimliliğini ve sürdürülebilirliğini önemli ölçüde artırmaktadır. Bu derleme, sürü yönetim sistemlerinin, otomasyonun ve yapay zekâ uygulamalarının evrimini ve yenilikçi avantajlarını özellikle süt sığırcılığının karmaşık bağlamı içinde incelemeyi amaçlamaktadır.

Anahtar Kelimeler: Yapay zekâ, Sürü yönetimi, Hayvancılık.

1. Introduction

Animal husbandry has been an integral part of human economic activities since time immemorial. As society's awareness of the importance of balanced nutrition grew, animal breeding evolved into a multifaceted endeavor, giving rise to intensive livestock enterprises focused on optimizing the yields of meat, milk, wool, and eggs. In these modern enterprises, a paramount concern is the welfare of the animals, while technology and machinery are harnessed to achieve this goal (1, 2).

In such livestock enterprises, an array of tasks, from herd management and insemination pairings to addressing temperature stress and fertilizer management, from maintaining udder health to monitoring estrus and fertility, as well as observing animal behavior and selection, are now conducted in digital environments. Modern animal husbandry encompasses the meticulous collection of data on productivity, behavior, and disease. Electronic identification materials, such as RFID tags, sensors, and cameras attached to animals' ears, ankles, and necks, record an extensive range of information, including the number of ruminations, movements, heat cycles, live weights, birth times, lying and standing times, feed consumption, body condition scores, milk yield and characteristics, feeding times, body temperatures, and various other parameters (3-6). Moreover, mechanization has greatly improved efficiency through the

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use of milking units, total mixed ration (TMR) preparation machines, and calf feeding robots, all managed through automation infrastructure (7). While these technologies have revolutionized data collection in modern animal husbandry, the current data primarily provide insights into the present situation, lacking predictive or prescriptive capabilities for the future.

In dairy cattle farming enterprises, farm management is an especially intricate affair compared to other livestock operations. It demands a professional management style rooted in technical expertise, effective use of automation systems, and a keen ability to analyze the diverse data within a well-structured framework. Farm management is fundamentally about collaboration, organization, and specialization in farming activities, with the overarching goal of maximizing long-term profitability and achieving the enterprise's objectives (8).

Herd management within dairy cattle farming is of paramount importance, as it is a perpetual cycle that encompasses all stages from calf birth to their development into heifers and cows, as well as the tasks required for production and market readiness (9). The principal aim of herd management is to oversee the herd professionally, ensuring the welfare, comfort, and productivity of the animals. Irrespective of the herd size, these enterprises systematically gather information about various aspects of their animals, evaluate it based on their intended purposes, and make informed decisions for the betterment of the enterprise. This cycle is reiterated annually. The success of the enterprise hinges on the decisions made by the herd management business manager, encompassing goal setting, resource allocation, planning, implementation, assessment, and review (10). Within the enterprise, key managerial units should be established, including those for production, business, finance, marketing, employees, and data acquisition and analysis. It is the responsibility of the business owner to make crucial decisions in a timely and effective manner, ensuring the establishment and profitable operation of these enterprises by orchestrating necessary adjustments, preparations, measurement and evaluation, implementation, and activities (11).

The farm manager is instrumental in making these decisions within the broader framework of these goals, which often involve setting specific objectives. In farm management, there is no one-size-fits-all approach, as the farm manager must employ the most suitable problem-solving methods and stay attuned to developments that provide optimal solutions to their questions. While farm management practices may exhibit some regional variations, they are ultimately bound by a global economic context, necessitating an awareness of both local and global sector developments. Like crop production, human, physical, and economic factors play pivotal roles in animal production (12). Managing dairy cattle enterprises and herds today is a complex task that demands expertise across multiple domains, including zootechnics, production, human resources, and marketing. In this competitive environment, it underscores the crucial need for experienced individuals who have dedicated themselves to this field (13). A competent business manager should possess the ability to promptly access essential information and bridge knowledge gaps effectively.

Achieving sustainable success in herd management goes beyond just managerial skills; it necessitates the comprehensive assessment of factors such as capital, labor, and the productive potential of the animals in question. Agriculture and animal husbandry play pivotal roles in providing humanity's fundamental food needs. In Turkey, bovine and ovine breeding are conducted either together or separately, depending on regional and ecological considerations. Dairy cattle breeding holds a prominent position in the Turkish economy (14). Operating dairy cattle enterprises entails a profound understanding, skill set, capabilities, and financial resources for tasks like enterprise management, herd management, animal care and feeding, product diversification, and marketing (15).

Livestock automation systems are instrumental in a range of areas, serving purposes such as minimizing errors stemming from human intervention due to the dairy cattle industry's sensitivity, optimizing costs under current conditions, diagnosing animal ailments, conducting daily care and feeding efficiently, ensuring safe product retrieval from production, enhancing animal welfare, monitoring estrus and pregnancy, evaluating animal behavior, tracking production levels, and ensuring food safety and health (16). These automation systems are primarily integrated into herd management systems. Given the intensification of dairy cattle farming, herd management has become increasingly intricate for business owners. To make well-informed decisions concerning the herd, it is essential to gather more data on individual animals (17). Technological applications have transformed herd management from a group-oriented approach to an individual-focused one (18). These technological applications enable constant oversight of the production process by employing automatic animal recognition, detection, measurement, and computing technologies. This, in turn, optimizes outcomes related to profitability, health, quality, product safety, animal welfare, and environmental conservation (19). When information technology, particularly computers, forms the backbone of herd management systems, they are often referred to as computer-aided herd management systems. The components integrated into these systems include electronic animal identification systems (RFID), automated milk measurement integrated into milking systems, automatic animal weighing systems, activity meters, automated intensive feed units, roughage and water consumption measurement systems, feed mixers with electronic scales, image analysis systems,

ultrasonographic imaging devices, yield analysis systems, herd management software, and internet connectivity (20).

Herd management systems implemented in dairy cattle breeding play a pivotal role in promoting sustainable milk production within the enterprise. They offer economic and ecological advantages while upholding high standards of environmental preservation, animal welfare, and consumer protection, along with ensuring top-tier quality benchmarks (21). The adoption of herd management systems offers a multitude of benefits, including minimizing the physical and psychological burdens on breeders, enhancing the overall success of the enterprise, reducing risks, optimizing resource utilization, ensuring the animals' needs are met to the fullest extent, providing human support for herd management tasks, enabling early disease detection, reducing the reliance on medications through early diagnosis and preventative measures, and harnessing the full potential of individual animals (22). These systems also provide breeders with more reliable data for animal selection, herd projections, and future planning. In dairy cattle farms, the utilization of these systems holds immense economic significance, particularly with larger herd sizes. Advanced herd management systems should deliver both economic and technical benefits to breeders, animals, and consumers. To realize these benefits, it's imperative to effectively implement and fully utilize the system, actively incorporating the vast amounts of data collected from various animals swiftly and accurately into decision-making processes concerning herds and individual animals. Users should also demonstrate proficiency in utilizing the hardware and software components of these systems (8).

In the contemporary context, technological advancements have led to the replacement of manual labor by machines. Concurrently, the development of computer systems and software has introduced subject areas like herd management systems, robotic systems, and artificial intelligence applications into the realm of animal husbandry. The prevailing approach focuses on harnessing technology efficiently to minimize workforce reliance and human errors, thus ensuring maximum productivity based on an array of numerical data obtained through herd management systems. It has been established that artificial intelligence applications, image-processing-based systems, and autonomous farming systems have the potential to reduce human error significantly while substantially enhancing the speed and quality of farm production. Artificial intelligence systems capable of autonomous decision-making in existing farms can identify animal diseases, optimize production, and enhance animal feeding (23). This study underscores the benefits of herd management and artificial intelligence applications in livestock farms, particularly within the context of dairy cattle farming, in light of the burgeoning advancements in computer technology.

1.1. Herd Management in Livestock

Recent advancements in computerized data recording techniques have significantly improved herd management systems. These technologies have streamlined the monitoring of herd health, productivity, performance, and production parameters. A variety of computer software programs have been specifically designed for use in large herd operations. These programs aim to enhance farm management and maximize farm income by analyzing reproductive health in dairy cattle and estimating the costs associated with increasing dairy substitutes. These software packages have been tailored to work seamlessly on various microcomputers (24).

In herd management systems, all animals in the herd, including those born on the farm and those introduced from external sources, are recorded with the assistance of a technician. Daily events, such as births, deaths, measurements, weighings, health assessments, and feeding records, are meticulously entered into the herd management system by the relevant technician. Herd management systems, like herd follow-up, enable objective evaluation of farm management decisions regarding the herd, breeding, and health procedures. This evaluation is based on a solid foundation, allowing for the identification of any deficiencies or areas for improvement. For a herd management system to succeed, the farm must recognize its benefits and assess it comprehensively. Successful implementation of this computer-based system at the farm level and maximizing its benefits are contingent upon breeders receiving proper training in system usage. Veterinarians must provide regular consultancy services on the farm. (25, 26).

Under the herd management system, detailed records are kept on aspects such as animal births, live weights at various stages, yield characteristics, health-related data, daily feeding practices, and environmental influences. These records play a vital role in ensuring the future productivity and health of the herd. They support practices such as health management, feed supply, feeding programs, animal breeding strategies, quality milk production, worker performance monitoring, and tracking income and expenses. These systems not only reduce the need for human labor but also minimize the potential for human errors (27).

Through the effective use of electronic animal identification, detection, measurement, feeding applications, and record-keeping technologies integrated into herd management systems, especially in commercial and large dairy cattle operations, continuous control of production processes has been achieved. Consequently, optimal results in terms of profitability, health, quality, product safety, animal welfare, and worker productivity and health have been realized. These systems also incorporate advanced technologies for production, fertility control, product quality, nutrition,

reproduction, and animal health management in dairy cattle (28).

1.2. Automation in Animal Husbandry

When considering the spheres of economic management, labor, productivity, and cost, agriculture and animal husbandry assume paramount significance. However, these domains also present considerable complexities. In the contemporary context, marked by technological progress, the incorporation of automated management systems into these sectors has become an imperative, paralleling the adoption of automation in other industries. These systems assume a pivotal role in herd surveillance, optimization of economic efficacy, enhancement of animal health, delineation of augmented yields, assurance of production quality, and expeditious, accurate decision-making across extensive and commercially-oriented livestock enterprises (29, 30).

The reception of automated herd management and automation systems within dairy cattle breeding hinges decisively on their cost-effectiveness for practitioners. In other words, the economic feasibility of modern automatic herd management and automation systems in animal husbandry must be appraised to guide investment deliberations. Globally, a trend is discernible wherein automation has gained ground at various junctures of dairy farming. Central to this shift is the amelioration of labor costs and physical exertion (31). Automation has found favor due to its resonance with the contemporaneous trajectory toward fewer yet larger herds, slenderer profit margins relative to yesteryears, and the consistent advancement of cost-effective extant Technologies (32).

In the broader conceptualization, automation encompasses the utilization of machinery, control systems, and information technologies, with the overarching aim of heightening production efficiency Automation is conceived as a proactive approach to dairy farm management, endowing dairy farmers with the capability to oversee expansive herds, economize time, and garner perspicacious insights. It is crucial to underscore that automation systems and technologies, per se, do not proffer direct problem resolution but function as discerning indicators, revealing areas warranting amelioration. From this vantage point, automation confers an array of merits, including augmented profitability, enhanced animal welfare, amelioration of lifestyle, and fortification of milk quality (19).

Presently, the realm of herd management and integrated automation systems predominantly assumes a computerized character, whereby numerous corporate entities have engendered software tools tailored for deployment in agricultural establishments of the livestock domain. Recent iterations of these software packages span diverse categories, encompassing breeding-focused software, programs oriented toward livestock breeding and comprehensive data capture, management, and accounting software purposed for the perpetuation of current records spanning the pivotal facets of cattle husbandry (33).

These software solutions have instituted the integration of supplementary elements into herd management systems. These include electronic animal identification, quantification of milk yield, timing of milking processes, measurement of milk flow rates, evaluation of milk electrical conductivity, and the assimilation of automated milk measurement systems into the milking framework, thereby affording data pertinent to milk temperature. Moreover, ancillary components involve activity meters, automatic animal weighing systems, estrus tracking systems, automatic mixed-feed units, feeder systems equipped with instrumentation for measuring roughage consumption, water consumption-measuring drinker systems, roughage-intensive feed mixers and distributors equipped with electronic scales, image analysis systems, and data analysis systems (19, 34).

Automation technologies usher in a regime of precise data accrual at the level of individual animals on agricultural holdings, thereby facilitating the efficacious management of larger herds. Herd management systems are underpinned by state-of-the-art instruments that accumulate data, thereby furnishing farm custodians with the informational substratum requisite for judicious decision-making. The systematic elucidation of these systems, as delineated by Schulze et al. (2007) and Rutten et al. (2013), unfolds across four key phases (35, 36):

Sensors, tasked with data generation through the measurement of specific parameters pertaining to the animals, for instance, cow activity.

An algorithm, which harnesses sensor data to yield informational insights concerning the animals. In this stage, raw or processed sensor-derived data may be amalgamated with non-sensor data.

A managerial decision-making framework, which synthesizes information from the antecedent phase with supplementary data, spanning technical, economic, and comparable domains. The culmination of this phase yields actionable recommendations.

The execution of decisions, which transpires either through the agency of the farmer or autonomously via the system, exemplified by the management of a cow's access to a milking robot.

However, it is requisite to acknowledge that these systems exhibit certain limitations. These limitations encompass the interpretational intricacies inherent in the data emitted, a consequence of the distinctiveness of each cow, in conjunction with the challenge posed by the notable volume of false alarms, impeding the pragmatic implementation of

extant models for disease and mastitis detection, grounded in data collated by various sensors (e.g., milk yield, electrical conductivity, activity, and analogous parameters) (36). Decision-making should rest upon a foundation of cogent scientific principles and standardized operating procedures intertwined with the intelligence proffered by the herd management system. Beyond these, key determinants that galvanize the functionality of these systems in agricultural settings span the spheres of investment costs, socio-economic dimensions, time considerations, and the anticipated return on investment (35).

1.3. Artificial Intelligence in Animal Husbandry

The early stages of the industrial revolution aimed to develop machinery capable of substituting human physical strength. With the advent of industrialization, various purpose-built machines were introduced into society, gradually replacing human labor over centuries due to their superior performance. As technology continued to advance, the realm of human work and cognitive processes saw a transformation through the integration of artificial intelligence (AI) techniques. AI is a method designed to create devices that mimic the functionality of the human brain, understanding how the human brain functions, processes sensory input, interprets stimuli, and draws conclusions based on stored knowledge. Following data reception, these AI systems can generate responses by formulating novel ideas and offering the best possible solutions. Current examples of such AI-powered devices or machines include computers and robots. AI approaches endeavor to replicate human-like intelligence and problem-solving capabilities in machines (37).

In the context of digital agriculture, AI plays a pivotal role in the application and integration of digital data, sensors, and tools throughout agricultural practices, spanning from the farm to the end consumer. This technology encompasses various components, including big data, sensor technology, sensor networks, remote sensing, robotics, and unmanned aerial vehicles (UAVs). The processing of collected data is now achieved through cutting-edge technologies like computer vision, machine learning, and artificial intelligence, among other methods. The application of AI is poised to benefit not only high-tech systems like milking equipment but also traditional dairy farms, enhancing their competitiveness in the future (38).

An illustrative study demonstrates the use of AI in regulating the ambient temperature for animals through water spraying, reducing heat stress. To implement this cooling system, an AI system leverages data from meteorological stationsand information about individual cows, combined with environmental factors. This system automatically adjusts the cooling parameters to meet desired volume and milk quality thresholds in dairy farms based on relevant data. Additionally, the system autonomously controls gates to direct individual cows to cooling systems with water sprinklers to mitigate heat stress or to standard milking parlors (39)

Biometric sensors are pivotal in herd management technologies and automation systems. They continuously monitor the health and behavior of individual animals in real time, enabling farmers to integrate this data for population-level analysis. Real-time data from these biometric sensors can be processed through big data analytics systems using statistical algorithms, yielding trend models and decision-making tools that empower breeders (40). These technologies facilitate secure and verifiable traceability of animal products from farm to consumer, offering a significant advantage in disease outbreak monitoring, economic loss prevention, and food-related health issues. They contribute to greater transparency in animal production, fostering increased consumer confidence. To harness the full potential of next-generation technologies, predictive analytics platforms are required, capable of sifting through vast datasets with a high degree of confidence while accommodating specific variables accurately and accessibly. Additionally, addressing data privacy, security, and integration issues remains paramount (41).

The agricultural sector is presently in the midst of a rapid digital transformation, with increasingly sophisticated technologies such as artificial intelligence (AI) and computer vision taking center stage. Within this context, computer vision, a fundamental facet of AI, has emerged as a pivotal enabler of precision agriculture. By harnessing high-quality imagery captured by remote cameras, computer vision has facilitated the automation of various agricultural operations, ushering in the era of smart agriculture. In particular, computer vision methodologies, in conjunction with herd management and automation systems, are being comprehensively employed to furnish comprehensive insights into the health and performance of individual animals (29). Such systems offer real-time data that aids farmers in making strategic decisions. Notably, recent research has focused on the implementation of computer vision for the recognition of livestock behaviors, exemplified by the works of Bello et al. (2021), Kumar et al. (2017), Qiao et al. (2019), and Shen et al. (2020) (42-45). For instance, a notable study by Xiao et al. (2022) involved the use of a modified Mask-RCNN model, trained through the fusion of Mask-RCNN and support vector machines (SVM), to identify cows within a barn (46).

Conventional animal record-keeping on medium-sized farms has been characterized by a time-intensive process. In contrast, contemporary methods involve the widespread use of small chips implanted within animals, which can be promptly scanned when the animals pass through a reader or designated location. This approach enables the computerized retrieval of pertinent information, including details related to

age, breed, sex, pedigree, and health records, offering a marked improvement in efficiency relative to traditional record-keeping practices. Furthermore, the advent of ultrasound technology has revolutionized the precise determination of pregnancy in inseminated cattle and the diagnosis of a spectrum of animal maladies (37).

As the awareness of animal welfare and emotional states in farm animals continues to mount, there exists an imperative to develop effective and precise monitoring techniques. Presently, there is a notable dearth of scientifically validated criteria for the quantification of transient emotional states in farm animals, as well as a conspicuous absence of established metrics for the assessment of animal well-being. Biometric sensor data, driven by AI, is emerging as a non-invasive solution for the monitoring of livestock. Notably, social network analysis has begun to gain traction as a means of modeling emotional dynamics and contagion among animals, facilitating the collection of extensive data pertaining to livestock emotions at the group level. AI technologies are playing a pivotal role in recognizing and comprehending the emotional states of animals, thereby facilitating improvements in their well-being and overall productivity (29).

Recent research endeavors have been directed towards the modeling of physiological responses in Holstein Friesian cows, encompassing parameters such as rectal temperature and respiratory rate, through the utilization of neural networks grounded in AI and neuro-fuzzy networks. These models exhibit predictive capabilities with regard to these physiological variables and, as such, have the potential to contribute significantly to the decision-making process (40). Moreover, contemporary investigations have explored the application of computer vision and machine learning for the prediction of parameters including heart rate, respiratory rate, eye temperature, milk production, and quality. These technologies have demonstrated efficacy in the enhancement of animal welfare and stress monitoring (40)

Traditional visual health assessments conducted by professionals and veterinarians can be inherently subjective, costly, and necessitate the presence of trained personnel. Recent advances in remote sensing, computer vision, and AI have paved the way for the development of innovative biometric techniques for the assessment of livestock health and welfare. Additionally, these techniques serve to facilitate livestock identification for the purposes of traceability, as well as the integration of machine and deep learning methodologies to tackle complex challenges encountered within the realm of livestock farming. Notwithstanding prior research efforts primarily centered on model development, there exists an exigent need for the formulation of more efficient, non-invasive, and dependable AI-driven techniques geared towards the assessment of animal health, welfare, and productivity. In this context, it is crucial to advocate for multidisciplinary team collaboration during the stages of model development and deployment, alongside the seamless integration of emerging digital technologies with AI development and deployment strategies. Such an approach is poised to facilitate the efficacious and scalable deployment of AI applications within the domain of animal husbandry (37).

2. Discussion and Conclusion

In conclusion, enhancing productivity and profitability within the realm of animal husbandry necessitates the precise evaluation of the extensive data at our disposal and the ability to make forward-looking predictions. Modern animal husbandry often relies on mechanistic models to assess data within the constraints of the specific system under investigation. These models, however, are primarily valuable for addressing intricate issues with a limited number of variables. The resolution of complex challenges in animal husbandry entails the systematic collection and analysis of vast datasets. To make accurate predictions and forecasts in livestock production, an array of diverse data sets, encompassing factors like weather, air quality, animal vocal signals, and visual animal behavior, must be collected. Given the impracticality of storing and processing such substantial volumes of text, audio, and video data using standard computers, there arises a pressing need for increased computing and storage capacity. This is precisely where Artificial Intelligence technologies, including sensors, big data, cloud computing, and machine learning algorithms, assume a pivotal role. The methodology devised to address business challenges or attain specific objectives, and the associated procedural steps, are collectively referred to as algorithms. Advanced Artificial Intelligence and Machine Learning Algorithms are harnessed for cloud-based analysis of big data, facilitating predictions of future events and recommendations for livestock managers. Big data analytics and machine learning algorithms scrutinize the collected data to detect deviations from standard models and offer insights into prospective developments. These insights can, in certain cases, trigger automated actions, providing individuals with the information needed to make informed decisions. Consequently, the integration of machine learning and human expertise leads to mutually informed decisions. Moreover, the application of these technologies enables the early detection of various diseases by monitoring irregular body movements and diminished activity in animals. The use of artificial intelligence in animal husbandry presents a solution to challenges that may be exceedingly challenging or even insurmountable through conventional means. This not only safeguards animal health but also drives up productivity, thereby ensuring the profitability and sustainability of livestock enterprises.

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Derlemeler / Review Articles

Taylarda *Rhodococcus Equi* Enfeksiyonunda Antibiyotik Kullanımı

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Özet: *Rhodococcus equi* taylarda yüksek oranlarda ölümlere neden olabilen hücre içi bir mikroorganizmadır. Öncelikle akciğerlerde lezyonlara neden olmakla birlikte diğer organlarda da etkili olabilmektedir. In vitro şartlarda birçok antibiyotik etkili olarak belirlenmekle birlikte tedavide çok azı kullanılabilmektedir. Atlarda sınırlı sayıda antibiyotik kullanımı tedaviyi güçleştirmektedir. Bu derlemede taylarda *Rhodococcus equi* enfeksiyonunda kullanılan antibiyotikler (eritromisin, rifampisin, vs) hakkında bilgiler verilmeye çalışılmıştır.

Anahtar Kelimeler: *Rhodococcus equi*, tay, antibakteriyel, tedavi

Use of Antibiotics in *Rhodococcus Equi* Infection in Foals

Abstract: *Rhodococcus equi* is an intracellular microorganism that can cause high rates of death in foals. Although it primarily causes lesions in the lungs, it can also affect other organs. Although many antibiotics have been determined to be effective under in vitro conditions, very few can be used in treatment. The limited use of antibiotics in horses makes treatment difficult. In this review, it can be tried to give information about the antibiotics (erythromycin, rifampicin, etc.) used in *Rhodococcus equi* infection in foals.

Keywords: *Rhodococcus equi*, foal, antibacterial, treatment

1. Giriş

Pnömoni taylarda ölüm nedenleri arasında ilk sıralarda bulunmaktadır. Taylarda birçok mikroorganizma solunum yolu enfeksiyonuna neden olmakla birlikte *Rhodococcus equi* etkeni pnömoninin en yaygın nedeni arasında bulunur. Önceki yıllarda *Corynebacterium equi* olarak isimlendirilen etken gram pozitif, makrofajlar içinde hayatta kalabilen ve çoğalabilen fakültatif bir hücre içi patojendir. Tedavi edilmediği vakalarda ölüm oranı %70'lere kadar çıkabilmektedir. Enfeksiyon genellikle subklinik seyrettiği için hastalık ileri dönemlerinde teşhis edilebilmektedir. Enfeksiyonda en fazla apseli pyogranülomatöz bronkopnömoni gözlenebildiği gibi bakteriyemi ve kronik bronkopnömoni de gözlenebilmektedir. Ancak *Rhodococcus equi* akciğer dışı bölgelerde de lezyonlara neden olabilmektedir. Enfekte tayların büyük kısmında sindirim sistemi lezyonları gelişmektedir. Sindirim sisteminde multifokal ülseratif enterokolit ve mezenterik veya kolon lenf düğümlerinde granülamatoz veya supratif yangı gelişir. Bazı hastalarda ise peritonit, polisinovit, septik artrit, osteomiyelit, üveit, sellülit, deri altı apse, nefrit ve karaciğer ile böbrek apseleri de oluşabilmektedir. Bazı vakalarda ise akciğer ve sindirim sisteminde belirti oluşmaksızın sadece septik artrit ve osteomiyelite neden olabilmektedir (1-5).

Taylar dışında kediler (6) ve köpeklerde (7) de *Rhodococcus equi* kaynaklı akciğer enfeksiyonunun gelişebildiği belirlenmiştir. Rhodococcal enfeksiyonlar zoonoz özellik göstererek insanlarda da gözlenebilmektedir. Özellikle immun depresan insanlarda bu etkene bağlı pnömoni enfeksiyonları tespit edilebilmektedir (8). AIDS/HIV hastalarında *Rhodococcus equi* tespit edildiği ve uzun süreli antibiyotik tedavisine ihtiyaç duyulduğu ifade edilmiştir (9, 10).

2.Kullanılan Antibiyotikler

In vitro şartlarda *Rhodococcus equi'* nin eritromisin, telitromisin, azitromisin, klaritromisin, gamitromisin, rifampisin, vankomisin, imipenem, gentamisin, doksisiklin, linezolid ve enrofloksasine duyarlı olduğu belirlenmiştir (4). *Rhodococcus equi* ile enfekte at makrofajlarında enrofloksasin, gentamisin ve vankomisin en etkili ilaç olduğu bildirilmiştir (11). Ancak klinik pratikte bu ilaçların hepsinin kullanımı yapılamamaktadır. Etkenin hücre içi olması, antibiyotiklerin kondrotoksik etkileri ve atlarda ölümcül kolite neden olabilmesi kısıtlayıcı faktörlerdir (2, 12).

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Taylarda azitromisin 10 mg/kg dozunda intragastrik (IG) uygulama sonrasında biyoyararlanımın %56, Tmax (Maksimum Konsantrasyona Ulaşma Süresi) değerinin 1.8 saat, Cmax (Maksimum Plazma Konsantrasyon) değerinin 0.57 mcg/mL olduğu, taylarda belirgin yan etkiler gözlenmediği ve 10 mg/kg dozun *Rhodococcus equi* tedavisinde yeterli doz olduğu ifade edilmiştir (13). Aynı dozda oral (PO) uygulama sonrasında biyoyararlanımın %39, Cmax değerinin 0.72 mcg/mL, Tmax değerinin 1.4 saat, yarı ömrün 18 saat olduğu, belirgin yan etkiler gözlenmediği ve uygulanan dozun tedavi için yeterli olabileceği bildirilmiştir (14). Taylara 6 mg/kg dozunda kas-içi (IM) olarak gamitromisin uygulaması sonrasında Cmax değerinin 0.333 mcg/mL, Tmax değerinin 1 saat, yarı ömrün 39 saat olduğu ve 6 mg/kg (IM) dozunda haftada bir sefer uygulamasının *Rhodococcus equi* tedavisinde etkili olabileceği bildirilmiştir (15). Taylara 10 mg/kg dozunda IG yolla klaritromisin uygulaması sonrasında Tmax değerinin 1.5 saat, Cmax değerinin 0.92 mcg/mL, yarı ömrün 4.8 saat olduğu, 7.5 mg/kg (PO, günde iki defa (BID) dozun yeterli olduğu ve belirgin yan etki gözlenmediği bildirilmiştir (16). Taylara 15 mg/kg dozunda telitromisin IG yolla uygulanması sonrasında Tmax değerinin 1.75 saat, Cmax değerinin 1.43 saat, yarı ömrün 3.81 saat olduğu ve *Rhodococcus equi* tedavisinde 15 mg/kg (PO, günde bir defa (SID) dozun yeterli olduğu ifade edilmiştir (17). Lipozomal gentamisinin taylara damar içi uygulaması ile yapılan farmakokinetik çalışmada yüksek derecede hücre içi konsantrasyona ulaştığı ve gelecekte *Rhodococcus equi* enfeksiyonlarının tedavisinde düşünülebileceği belirtilmiştir (18). Taylara doksisiklin 10 mg/kg dozunda IG yolla uygulaması sonrasında yarı ömrün 8.48 saat, Tmax değerinin 3 saat, Cmax değerinin 2.54 mcg/mL olduğu ve 10 mg/kg dozda BID olarak uygulamanın tedavide yeterli olabileceği ifade edilmiştir (19).

Taylar deneysel yöntemle *Rhodococcus equi* enfeksiyonu tedavisi ile ilgili çalışmalar oldukça sınırlıdır. Bunun nedeni olarak etik sorunlar, yüksek maliyet ve modelin oluşturulması ile ilgili teknik zorluklar gösterilmektedir. Ayrıca çalışma sonuçlarının etkenin virülansına, aşılamaya, tayın yaşına ve önceden maruziyete bağlı olarak değişebilmektedir. *Rhodococcus equi* taylarda genellikle subklinik akciğer lezyonları ile seyretmekte olduğu için tedaviye ihtiyaç duyulmadan iyileşmeler gözlenebilmektedir. 1980'lerden günümüze *Rhodococcus equi* ile enfekte olmuş taylar için standart tedavi önerisi, bir makrolidin (eritromisin, klaritromisin, azitromisin veya gamitromisin) rifampisin ile kombinasyonu olmuştur (3, 4). Ancak makrolidler ile rifampisine yüksek derecede direnç geliştiği ve yeni tedavi protokolleri düşünülmesi gerektiği de bildirilmektedir (20, 21, 22). Tedaviye başlamadan önce antibiyogram yapılması da önerilebilmektedir (23). Genel olarak tedavide eritromisin estolat/etilsüksinat (25 mg/kg, PO, günde üç defa (TID)-günde dört defa (QID) + rifampisin (5-7.5 mg/kg, PO, BID veya 10 mg/kg, PO, SID) uygulaması 4-9 hafta yapılır (2, 3). Rifampisinin uzun süreli oral uygulanması sonrasında genellikle ciddi yan etkiler gelişmediği, ancak parenteral uygulamalarda ciddi yan etkiler gözlenebildiği ifade edilmiştir. Eritromisin uygulaması esnasında taylar enterit yönünden kontrol altında tutulmalıdır. Gelişebilecek dışkı yumuşaması veya hafif ishallerde tedaviye ara verilmesi gerekmemektedir. Ancak ciddi sıvı kaybı, depresyon ve dehidratasyon oluştuğunda ilaç uygulaması durdurulmalıdır (2, 3, 12, 24). Ayrıca rifampisin (5 mg/kg, PO, BID) + klaritromisin (7.5 mg/kg, PO, BID) 3-12 hafta, rifampisin (10 mg/kg, PO, SID) + azitromisin (10 mg/kg, PO, SID, 5-7 gün sonra 2 günde bir) 6 hafta, doksisiklin (10 mg/kg, PO, BID) + azitromisin (5 mg/kg, PO, SID) 6 hafta, tulatromisin (2.5 mg/kg, IM, haftada bir sefer) 6 hafta veya gamitromisin (6 mg/kg, IM, haftada bir sefer) 6 hafta uygulanabilecek diğer tedavi seçenekleridir (25, 26). Taylar bu ilaçların uygulamasından sonra ishal yönünden takip altında tutulmalıdır. Rhodococcal enfeksiyonunun tedavisinde antibiyotikler dışında bronkodilatör (terbutalin, aminofilin, klenbuterol), mukolitik (asetilsistein, bromeksin), nonsteroid antiinflamatuar (fluniksin meglumin, metamizol) ve sıvı-elektrolit tedavi de yapılmalıdır. Hastalara glukokortikoid uygulaması yapılmamalıdır. Klinik etkinliği kesin olarak ortaya konulamamakla birlikte, alternatif olarak insanlarda *Rhodococcus equi* enfeksiyonlarında kullanılan tedavi protokolü uygulanabileceği bildirilmiştir. Tedavide vankomisin + imipenem silastatin uygulaması en az 3 hafta yapılır ve rifampisin + eritromisin uygulaması ile devam edilir (2, 3, 12).

Gamitromisinin etkinliğinin rifampisin + azitromisin ile karşılaştırıldığı araştırmada, gamitromisinin bronkopnömoni tedavisinde rifampisin + azitromisin kadar etkili olduğu, ancak gamitromisinin daha fazla yan etkilere neden olduğu bildirilmiştir (27). Taylarda *Rhodococcus equi* kaynaklı akciğer enfeksiyonunun tedavisinde tulatromisin etkinliğinin, azitromisin + rifampisin kombinasyonu ile karşılaştırıldığı çalışmada, tulatromisinin etkinliğinin kombinasyondan daha düşük olduğu ifade edilmiştir (28). Yapılan benzer başka bir çalışmada taylarda *Rhodococcus equi'* nin neden olduğu pulmoner apselerin tedavisi için tulatromisin, azitromisin veya azitromisin + rifampisin kombinasyonunun etkinliğinin kıyaslandığı araştırmada azitromisinin tek başına veya rifampisin ile kombinasyonunun daha etkili olduğu belirtilmiştir (29). Taylarda *Rhodococcus equi* 'nin neden olduğu pnömoninin tedavisinde azitromisin + rifampisin, klaritromisin + rifampisin veya eritromisin + rifampisinin etkinliğinin karşılaştırıldığı araştırmada klaritromisin + rifampisin kombinasyonunun daha etkili olduğu ifade edilmiştir (30). Taylarda *Rhodococcus equi* kaynaklı bronkopnömoni tedavisinde azitromisin + doksisiklin kombinasyonunun azitromisin + rifampisin kombinasyonu kadar etkili olduğu belirtilmiştir (31).

Günümüzde Türkiye'de satışta aşı bulunmamaktadır. Ancak antibiyotik uygulaması dışında taylara *Rhodococcus equi* hiperimmun plazma uygulamasının olumlu etkileri bildirilmiştir (32, 33).

3. Sonuç ve Öneriler

- Taylarda *Rhodococcus equi* enfeksiyonlarının tedavisinde eritromisin + rifampisin kombinasyonu ilk seçenek olarak düşünülebilir.
- Eritromisin yerine azitromisin veya klaritromisin değerlendirilebilecek diğer makrolid antibiyotiklerdir.
- Tedavi süresince hastalar antibiyotiğe bağlı ishal yönünden sürekli kontrol edilmelidir.
- İn vitro şartlarda etken birçok antibiyotiğe duyarlılık göstermekle birlikte in vivo şartlarda yeterince etkileri olmaması ve atlarda ağır yan etkiler göstermeleri nedeni ile kullanımları kısıtlanmaktadır.
- Destekleyici tedaviler (bronkodilatör, mukolitik, nonsteroid antiinflamatuar) ve sıvı-elektrolit) başarı oranını arttırabilmektedir.
- Genel olarak antibakteriyel tedavide etkili başarı elde edilebilmesi için etken izolasyonu ve antibiyogram testleri dikkate alınmaktadır. Ancak *Rhodococcus equi* etkeni in vitro şartlarda birçok antibiyotiğe duyarlılık gösterebilmektedir. Bu durumda klinikte uygulanması düşünülen antibiyotiğin hücre içi yaşayan bu etkene ulaşacak şekilde lipofilik ve etkeni spektrumu içine alabilen özelliklere sahip olması gerektiği klinisyenlerce akılda tutulmalıdır.

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BOZOK VETERİNER BİLİMLERİ (BOZOK VET BİL)
YAZIM KURALLARI

AMAÇ

Bozok Veteriner Bilimleri'nde, Veteriner Klinik Bilimleri, Veteriner Klinik Öncesi Bilimleri, Veteriner Temel Bilimleri, Gıda Hijyeni ve Teknolojisi, Zootekni ve Hayvan Besleme alanlarında hazırlanmış güncel ve özgün değeri olan orijinal araştırma makaleleri, olgu sunumları, derlemeler, kısa bildiriler ve editöre mektuplar yayımlanarak ulusal ve evrensel bilime katkı sağlamak amaçlanmıştır.

KAPSAM

Bozok Veteriner Bilimleri Yozgat Bozok Üniversitesinin bilimsel yayın organı olup Haziran ve Aralık aylarında olmak üzere yılda iki kez yayımlanır. Derginin kısaltılmış ismi 'Bozok Vet Sci'dir. Yayın hayatına 2020 yılından itibaren başlayacak olan Bozok Veteriner Bilimleri hakemli ve bilimsel süreli dergi olarak yayınlanacaktır.

Dergimizde, Türkçe ve İngilizce dillerinden birinde hazırlanmış olan ve daha önce başka bir dergiye eş zamanlı olarak sunulmamış Veteriner Klinik Bilimleri, Veteriner Klinik Öncesi Bilimleri, Veteriner Temel Bilimleri, Gıda Hijyeni ve Teknolojisi, Zootekni ve Hayvan Besleme alanlarında hazırlanmış orijinal araştırma makalesi, olgu sunumu, davetli ve editör onayı alınmış derlemeler, kısa bildiriler ve editöre mektuplar yayınlanır.

YAZIM KURALLARI (MAKALENİN-YAZININ HAZIRLANMASI)

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10. Bozok Veteriner Bilimleri'ne gönderilen yazılar, aşağıdaki sıraya göre (Başlık, Özet, Metin, Kaynaklar, Tablolar ve Şekiller) düzenlenmeli, Tablo ve Şekiller ayrı sayfalarda belirtilmelidir.
11. Dergiye gönderilen çalışmalar Abstract, Özet, Giriş, Materyal ve Metot, Bulgular, Tartışma ve Sonuç, Kaynaklar başlıklarından oluşmalıdır. Giriş, Materyal ve Metot, Bulgular, Tartışma ve Sonuç bölümleri numara verilerek belirtilmelidir (1.Giriş, 2.Materyal ve Metot, 3.Bulgular, 4.Tartışma ve Sonuç). Alt başlıklar 1.1., 1.2., şeklinde ardışık olarak numaralandırılmalıdır. Referanslar bölümü numaralandırılmamalıdır.

a. Başlık: Başlık kısa, açık, tüm harfleri büyük ve yazı için uygun olmalıdır. Özellikle elektronik sunumda makalenin sadece başlığı, (yazar ve kurum adresi vermeksizin) yazılmalıdır. Bu yöntem, yazıların uzmanlarca tarafsız bir şekilde değerlendirilmesini sağlamak amacıyla uygulanmaktadır.
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altına 4-6 adet anahtar kelime verilmelidir. Türkçe anahtar kelimeler "Türkiye Bilim Terimleri (TBT)"ne uygun olarak verilmelidir (Bkz. http://www.bilimterimleri.com). İngilizce anahtar kelimeler "Medical Subject Headings (MESH)" e uygun olarak verilmelidir (Bkz. http://www.nlm.nih.gov/mesh/MBrowser.html).

c. Metin: Araştırma makalelerinde; Giriş, Materyal ve Metot, Bulgular ile Tartışma ve Sonuç bölümleri, olgu sunumlarında ise; Giriş, Olgu Sunumu, Tartışma ve Sonuç bölümleri olmalıdır. Bölüm başlıkları ilk harfi büyük olacak şekilde küçük harfler ile yazılmalıdır. Yazılarda "Systeme International (SI)" birimleri kullanılmalıdır. Derleme makaleler için hazırlanan özet derlemenin konusu hakkında bilgi ve derlemenin amacından oluşmalıdır. Derleme makalesi "Giriş" ile başlamalı, yazar/lar tarafından belirlenecek ara başlıklarla devam etmeli, "Sonuç" ve ''Kaynaklar'' ile tamamlanmalıdır.

d. Sembol, birim ve kısaltmalar: Dergimiz, *Scientific Style and Format, The CSE Manual for Authors, Editors, and Publishers*, Council of Science Editors, Reston, VA, USA (7th ed.) tarafından belirtilen sistemi kabul etmektedir. ×, μ, η, veya ν gibi semboller MS Word sembol listesinden seçilerek kullanılmalıdır. Derece (°) sembolü gösterimi için; "O" harfinin veya "0" rakamının üst simge şeklinde gösterilmesi ile yapılmamalı sembol menüsünden kullanım tercih edilmelidir. Çarpım "x" harfi değil sembol menüsü (×) kullanılmalıdır. Sayı, birim ve matematiksel semboller (+, –, ×, =, <, >), kullanıldıktan sonra bir boşluk bırakılmalı (örneğin., 3 kg), yüzde işaretinden sonra boşluk bırakılmamalıdır (örneğin, %45). Latince et al., in vitro veya in situ terimleri italic olarak gösterilememelidir.

e. Kaynaklar: Kaynaklar metin içinde parantez içinde numara ile belirtilmelidir. Birden fazla kaynağa atıf yapılacaksa aynı parantez içerisinde belirtilmelidir örn, (3,5,7-11). Literatür listesinde yer alan kaynakların her biri için metinde atıf yapılmalıdır.

Beşten fazla yazarı olan kaynaklarda, beşinciden sonrası için "et al." eki kullanılmalı, aşağıda verilen sistematik ile noktalama işaretleri ve yazım kurallarına dikkat edilerek yazılmalıdır.

a. **Kaynak süreli yayın ise**; Örnek: Durmuş İ, Demirtaş ŞE, Can M, Kalebaşı S. Determining egg consumption habits in Ankara. Tavukçuluk Araştırma Dergisi 2007; 7: 42-45 (article in Turkish with an English abstract).
b. Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S et al. Antibiotic resistance: a rundown of a global crisis. Infection and Drug Resistance 2018; 11: 1645-1658. doi: 10.2147/IDR. S173867.
c. **Kaynak editörlü kitaptan bir bölüm ise**; Örnek: Gay CC, Besser TE. Escherichia coli septicaemia in calves. Gyles CL. eds. In: Escherichia Coli in Domestic Animals and Humans. Wallingford: CAB International, 1994; pp.75-90.
d. **Kaynak kitap ise**; Örnek: Varley H, Gowenlock AH, Bell M. Practical Clinical Biochemistry. Fifth Edition. London: William Heinemann Medical Books Ltd, 1984; p. 685.
e. **Kaynak editörlü kitap ise**; Örnek: Constable PD, Hinckliff KW, Done SH, Grunberg W. Veterinary Medicine. Eleventh Edition. London: W.B. Saunders Company, 2017; p.57.
f. **Kaynak kongre bildirisi ise**; Örnek: Kirbas A, Degirmencay S., Kilinc AA, Eroglu MS. Increased cardiac troponin-I concentration and cardiac enzyme activities in neonatal calves with sepsis. Second International Veterinary Internal Medicine Congress. October, 11-13, 2019; Ankara-Türkiye.
g. **Kaynak tez ise;** Örnek: Kırbaş A. Elâzığ, Samsun, Sivas, Tokat ve Yozgat illerindeki sığır ve koyunlarda Kırım Kongo Kanamalı Ateş virüs enfeksiyonunun seroprevalansının araştırılması, Doktora tezi, Fırat Üniv Sağ Bil Ens, Elâzığ 2009; s.1-2. (thesis in Turkish with an English abstract).

Web tabanlı erişimler kaynak olarak gösterilmemelidir.

f. Tablolar; kaynaklar kısmından sonra, her bir tablo ayrı sayfada olacak şekilde verilmelidir. Tablo başlıklarının yalnızca ilk harfleri büyük olmalıdır. Tablo başlıkları tablonun üzerinde bulunmalı ve **Tablo 1.** (**Table 1.**) şeklinde numaralandırılmalıdır. Tablolarda iç ve yan kılavuz çizgiler kullanılmamalıdır. Tanımlayıcı bilgi ve açıklamalar tabloların altına yerleştirilmelidir.

Örnek:

Table 1. Determination of elements in Dogfish Liver certified reference material

	Concentration (μg g^{-1})		
	Certified[a]	Found[b]	R(%)
Al[c]	200	215 ±10	108
V[c]	0.6	0.56 ± 0.01	93
Cr[c]	1.4	1.52 ± 0.02	109
Co[c]	0.25	0.28 ± 0.02	112
As	9.66 ± 0.62	9.55 ± 0.16	99
Cd	24.3 ± 0.8	24.2 ±0.3	100
Cu	31.2 ± 1.1	31.7±0.4	102
Fe	1833 ± 75	1914±65	104
Pb	0.16 ± 0.04	0.16±0.02	100
Hg	2.58 ± 0.22	2.31±0.02	90
Ni	0.97 ± 0.11	0.94±0.03	97
Se	8.3 ± 1.3	8.3±0.2	100
Ag	0.93 ± 0.07	0.86±0.01	92
Zn	116 ± 6	113± 1	97

[a] At 95 % confidence level

b $\bar{x} \pm SD$, n=3, [c]Information value

g. Her resim, grafik ve çizim; şekil olarak kabul edilip **Şekil 1.** (**Figure 1.**) gibi yazılmalı, her biri ayrı sayfada olacak şekilde verilmelidir. Tanımlayıcı bilgi ve açıklamalar şekil ismi ile birlikte şeklin altına yerleştirilmelidir. Resimler 300dpi çözünürlükte olmalıdır.

Örnek:

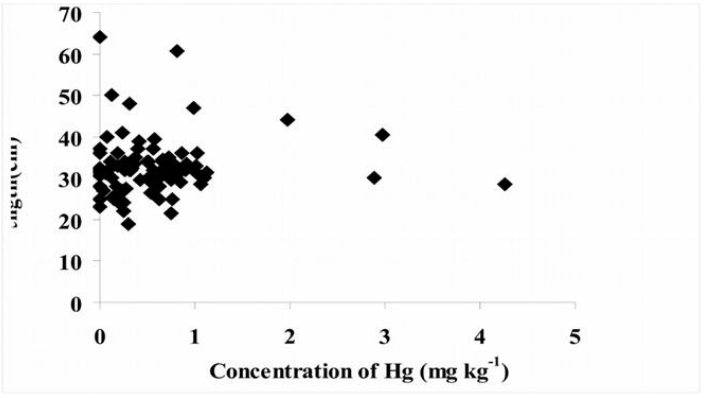

Figure 1. Concentration of Hg (mg kg^{-1})

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Purpose

In Bozok Veterinary Sciences, by publishing original research articles, case reports, reviews, short papers and letters to the editor with current and original value prepared in the fields of Veterinary Clinical Sciences, Veterinary Preclinical Sciences, Veterinary Basic Sciences, Food Hygiene and Technology, Animal Science and Animal Nutrition. It is aimed to contribute to national and universal science.

Scope

Bozok Veterinary Sciences is the scientific publication of Yozgat Bozok University and is published twice a year, in June and December. The abbreviated name of the journal is Bozok Vet Sci. Bozok Veterinary Sciences, which will start its publication life in 2020, will be published as a peer-reviewed and scientific periodical.

In our journal, an original research article, case report, prepared in the fields of Veterinary Clinical Sciences, Veterinary Preclinical Sciences, Veterinary Basic Sciences, Food Hygiene and Technology, Animal Science and Animal Nutrition, which was prepared in one of the Turkish and English languages and was not presented simultaneously to another journal, Invited and editor-approved reviews, short papers and letters to the editor are published.

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    b) Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S et al. Antibiotic resistance: a rundown of a global crisis. Infection and Drug Resistance 2018; 11: 1645-1658. doi: 10.2147/IDR. S173867.
    c) **If the source is a chapter from the edited book**; Gay CC, Besser TE. Escherichia coli septicaemia in calves. Gyles CL. eds. In: Escherichia Coli in Domestic Animals and Humans. Wallingford: CAB International, 1994; pp.75-90.
    d) **If the source book;** Varley H, Gowenlock AH, Bell M. Practical Clinical Biochemistry. Fifth Edition. London: William Heinemann Medical Books Ltd, 1984; p. 685.
    e) **If the source is an edited book**; Constable PD, Hinckliff KW, Done SH, Grunberg W. Veterinary Medicine. Eleventh Edition. London: W.B. Saunders Company, 2017; p.57.
    f) **If the source is the congress notice**; Kirbas A, Degirmencay S., Kilinc AA, Eroglu MS. Increased cardiac troponin-I concentration and cardiac enzyme activities in neonatal calves

with sepsis. Second International Veterinary Internal Medicine Congress. October, 11-13, 2019; Ankara-Türkiye

g) **If the source is thesis**; : Kırbaş A. Elâzığ, Samsun, Sivas, Tokat ve Yozgat illerindeki sığır ve koyunlarda Kırım Kongo Kanamalı Ateş virüs enfeksiyonunun seroprevalansının araştırılması, Doktora tezi, Fırat Üniv Sağ Bil Ens, Elâzığ 2009; s.1-2. (thesis in Turkish with an English abstract).

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Sample :

Table 1. Determination of elements in Dogfish Liver certified reference material

	Concentration (µg g^{-1})		
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Al[c]	200	215 ±10	108
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Zn	116 ± 6	113±1	97

[a] At 95 % confidence level

b $\overline{x} \pm SD$, n=3, [c]Information value

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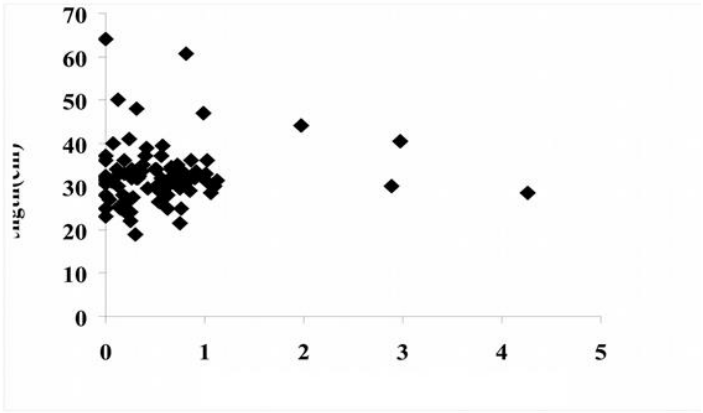

Figure 1. Concentration of Hg (mg kg^{-1})

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İçindekiler / Contents

2024, 5 (1)

Araştırma Makaleleri / Research Articles

Dereli ÖN, Gulmez M, Yıldız Bayhan K, Üner S. *Use of Raw, Thermized and Pasteurized Cow's Milk for Making Siirt Herby Tulum Cheese*.....1-9

Karadal F, Sakin-Şahin T, Bağcı C, Ertaş Onmaz N. *Quality Characteristics of Raw Milk Samples Purchased from Automatic Milk Vending Machines in Niğde Province*.....10-17

Olgu Sunumu / Case Reports

Erdogan S, Ak G, Erdogan H, Ural K. *Clinical Efficacy of Bleomycin in Suspected Canine Papillomatosis: Case Report of Two Sibling Puppies*.....18-22

Derlemeler / Review Articles

Yılmaz KB. *Advancing Dairy Cattle Farming: Integrating Herd Management, Automation and Artificial Intelligence for Elevated Productivity and Sustainable Practices*.....23-30

Uslu M ve Yazar E. *Taylarda Rhodococcus Equi Enfeksiyonunda Antibiyotik Kullanımı*.....31-34