Turkish Journal of Engineering
https://dergipark.org.tr/en/pub/tuje
e-ISSN 2587-1366

In vitro release kinetic and *in vivo* field trial performance of a long-term sustained-release bolus for Saanen goats

Gurbuz Comak [1], Murat Durmuş [2], İbrahim Erez [2]

[1] *Department of Chemical Engineering, Faculty of Engineering, Mersin University, Mersin, Türkiye; gcomak@mersin.edu.tr*
[2] *Department of Animal Science, Faculty of Agriculture, Cukurova University, Adana 01330, Türkiye;*
muratdurmus1991@gmail.com; ibrahimerz01@gmail.com

Cite this study: Comak, G., Durmuş, M., & Erez, İ. (2024). *In vitro* release kinetic and *in vivo* field trial performance of a long-term sustained-release bolus for Saanen goats. Turkish Journal of Engineering, 8 (4), 712-719.

https://doi.org/10.31127/tuje.1475109

Keywords
Bolus
Sustained-release
Saanen goat
Release kinetic

Research

Received: 29.04.2024
Revised: 21.05.2024
Accepted: 22.05.2024
Published: 31.10.2024

Abstract

Controlled release studies of sustained-release boluses are of critical importance as their application in ruminants has been varying from providing mineral and vitamin support to prevent the development of clinical problems such as hypocalcemia and ketosis. This study examines both morphological and kinetic release of a sustained-release bolus and its performance study on Saanen goats. The bolus was studied by the means of continuous flow rig which the artificial saliva was pumped through with a flow rate of 3 mL/min. In addition to zero order kinetic, there was no crack or deformation observed through the immersion times but erosion was present. Field trials conducted with a number of 28 Saanen goats show that the treatment group is of higher multiple birth rates than the control group. No triple birth was observed on the control group. However, the rate of change in the body weight significantly increased in twins and triplets compared to the control group.

1. Introduction

Alternative solutions in feeding of not only trace elements and minerals but also in administration of active drug ingredients through sustained-release boluses applications have been gaining attraction from academia and industry in recent decades. Application of two boluses at once significantly increased plasma copper concentration and blood glutathione peroxidase in both young age and adult cattle [1-3]. The release of Ivermectin from soluble silicate glass scaffolds in a sustained-released bolus formulation has been used in healing of small ruminants for the problems caused by parasites [4]. Commercially used boluses offer a number of benefits in compensation of trace mineral and vitamin deficiencies therefore bringing such benefits like weight gain and strengthening immune system in ruminants [5]. Especially in developing countries, the meat and milk production dependence on small ruminants is crucial [6]. Saanen goat is known to be as one of the best species in terms of milk production and breeding [7]. The productivity of dairy goats can be affected by different climatic conditions, including high temperatures [8-10]. Heat stress has a larger impact on dairy animals due to their higher metabolism [10-11]. This situation is more important in the Mediterranean region, where small ruminant breeding is common [12-13]. Heat stress causes a decrease in feed intake, a decrease in growth, fertilization rate, embryonic development and an increase in early embryonic deaths [8-9, 11, 14]. One of the ways to optimize animal production and reproduction is to use metabolic enhancers to minimize complications arising from stress conditions. Metabolic enhancers such as vitamins and minerals increase growth rate, improve feed efficiency and reproductive performance [15]. Trace elements and vitamins can have significant effects on fertility and reproductive performance [16]. Some vitamins (such as A and E), which are essential components of biological processes including fertility and embryonic development, can improve reproductive performance, reduce oxidative stress caused by mating and pregnancy, and protect fertility [17]. Deficiencies in Vitamins A and E and minerals of I, Cu, Mg, Mn and Se, cause quiescent estrus, anovulation, abortion, and the birth of lambs that are difficult to survive in some of cases [18].

In this study, the release kinetic of a commercial bolus was conducted in a continuous flow *in vitro* system and *in vivo* studies for the effect of its administration on Saanen goats were carried out. The effect of the long-term support of trace elements and vitamins on rump width, chest depth and rate of body weight change was studied.

2. Material and methods

2.1. Materials

2.1.1. Reagents used in artificial saliva

The granulated powder and bolus samples (Ramewe is a trade name of a long-term sustained-release bolus product) were provided from Vittek, Türkiye. The vitamin and mineral content of Ramewe bolus is given as follows; *Provided per kilogram of vitamin-mineral mixture: 5.350.000 IU vitamin A, 1.075.000 IU vitamin D3, 27.000 mg Vitamin E, 117.500 mg Beeswax, 235.000 mg Zn, 116.500 mg Mn, 33.500 mg I, 7000 mg Co, 4.000 mg Se.* The artificial rumen saliva was prepared based on the work of McDougal et. al. (1948) [19]. The following reagents were used as received; Ammonium phosphate bibasic ($(NH_4)_2HPO_4$) (reagent grade, ≥98.0%), Ammonium sulfate ($(NH_4)_2SO_4$) (ACS reagent, ≥99.0%), Magnesium sulfate heptahydrate ($MgSO_4 \cdot 7H_2O$) (ACS reagent, ≥98%), Potassium chloride (KCl) (ACS reagent, 99.0-100.5%), Casein hydrolysate (for microbiology), Acetic acid (glacial, ReagentPlus®, ≥99%), Urea (ACS reagent, 99.0-100.5%) and Hydrochloric acid (HCl) (ACS reagent, 37%) were purchased from Merck. Calcium chloride dihydrate ($CaCl_2 \cdot 2H_2O$) (ACS reagent, ≥99%), Sodium bicarbonate ($NaHCO_3$) (Food grade ≥99%), Cobalt chloride hexahydrate ($CoCl_2 \cdot 6H_2O$ - ACS reagent, 98%), L-Cysteine (for biochemistry), Biotin (≥99.0% (T)), p-amino benzoic acid (ReagentPlus®, ≥99%), Isobutyric acid (99.0%) and Valeric acid (≥99%, FCC, FG) were purchased from Sigma Aldrich.

2.1.2. Composition of feed ration

All the goats received the same TMR (total mix ration) throughout the field study twice daily at times 08:00 and 15:00 (feed ration, Table 1). The goats received 3.5 kg of the given total TMR daily along the study covering before and after the birth. After birth, the kids received only mother milk for two weeks, then mother milk and the TMR until up to two months of age. The kids stopped receiving the mother milk after two months. All the goats and kids included in the study consumed water freely under normal feeding and management conditions.

Table 1. Ingredients and nutrient composition of concentrate used in the study (dry in air).

Ingredients of feed[1]	TMR for the goats%	TMR for the kids%
Corn	41.4	24.85
Barley	11.3	6.79
Vibrotal	3.0	10.2
Soy bean meal (with 48% crude protein)	17.4	9.0
Wheat bran	7.5	4.53
Corn distillers dried grains with soluble (DDGS)	15.1	9.0
Molases	3.02	1.81
Fractionated oil	1.5	0.91
Salt	0.8	0.4
Vitamin-mineral mixture[1]	0.1	0.07
Sodium bicarbonate	0.8	0.75
Lime	1.1	40.0
Nutrient composition	**%**	**%**
Dry matter	89.53	91.1
Crude protein	18.30	17.2
Acid Detergent Fiber	6.64	8.48
Neutral Detergent Fiber	20.01	34.1
Crude fat	3.83	44.4
Crude ash	6.90	5.86

[1] Provided per kilogram of vitamin-mineral mixture: 15.000.000 IU vitamin A, 3.000.000 IU vitamin D3, 30.000 mg Vitamin E, 150.000 mg Niacin, 10.000 mg Cu, 800 mg I, 150 mg Co, 150 mg Se, 50.000 mg Mn, 50.000 mg Fe, 50.000 mg Zn, 6.800 mg organic Mn, 1.400 mg organic Cu, 6.800 mg organic Zn, 6.800 mg organic Fe, 50 mg organic Se.

2.2. Methods

2.2.1. Characterization of bolus samples

The particle size of the granulated powder form of bolus was determined by the means of the Nano ZS model Malvern Zetasizer. Weight loss of bolus was determined at a given time intervals by taking out the bolus from the immersed artificial saliva and freeze-dried in Teknosem TRS 2/2V [20]. The weight of bolus was measured to calculate the dissolution kinetics. The morphology of bolus samples were determined by the means of a FEI Quanta 650 FEG scanning electron microscope (SEM).

2.2.2. In vitro release kinetic study

Fig. 1 shows the schematic rig of the continued process. The general procedure for the release studies are as followed; A bolus was immersed by a membrane bag (729 woven polyester filter cloth, Hebei Macrokun) into a beaker with a volume of 3L. The artificial rumen saliva was continuously pumped (Shenchen BT100N peristaltic pump) with a flow rate of 3 mL/min. Outlet of the rig to collect the excess fluid was connected to a waste container. The mixing and temperature (39 ^{o}C) were accomplished by the means of a hot plate with magnetic stirring. The pH of the solution was measured in real time and kept at around 6.5 with an addition of 0.1M HCl solution throughout the test period if required. Arduino UNO (open source microcontroller board) was used to monitor and collect pH and temperature data. Distilled water obtained from A Milli-Q system (Millipore, Milford, MA, USA) was used.

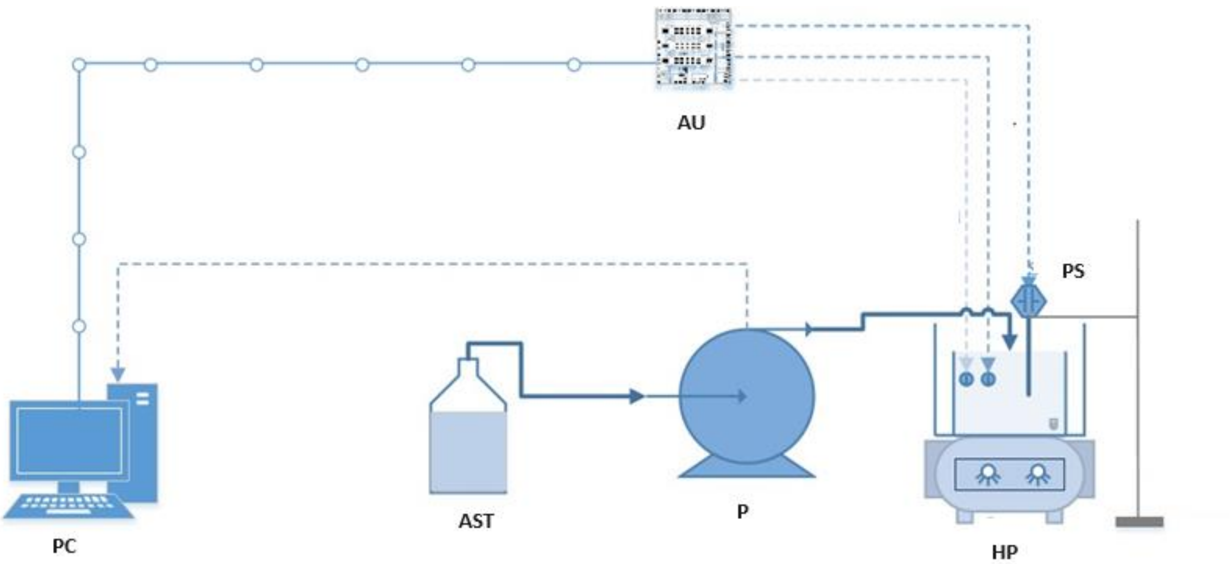

Figure 1. The schematic of continuous flow rig for the sustained-released studies. **PC**; Computer, **AST**; Artificial Saliva Tank, **P**; Pump, **AU**; Arduino UNO, **HP**; Hot Plate, **PS**; pH Sensor.

2.2.3. *In vivo* field study test

Field Trial Location and Environment: The research was carried out in the facilities of Çukurova University Faculty of Agriculture Dairy Goat Breeding Research and Application Farm, which has a semi-open pen system with an open south side in the east-west direction. Adana, where the study was conducted, is a province in the Mediterranean Region, located at 37º north parallel, 35º east longitude and with an altitude of 40 m above sea level. Summer months in the region are hot and dry, and winter months are warm and rainy. The average humidity is around 66%.

The Selected Animals and Application Details: 28 Saanen goats were divided into two groups: control and treatment groups. Care was taken to distribute trial material goats of the same age and similar live weight to the trial groups. A bolus was administered to the goats in the treatment group, 1 bolus per animal, 2 weeks before mating during the estrus period.

Feed Analysis: Samples were taken from the roughage and mixed feed used in the trials, and dry matter, crude protein, crude oil and crude ash analyses were performed according to the AOAC (2005) [21]. Neutral detergent fiber (NDF) and acid detergent fiber (ADF) analyses were carried out using a filter bag technique on a fiber analyzer (Ankom-200 Fiber Analyzer, ANKOM Technology Corp., NY) using temperature-resistant α-amylase and sodium sulfite as described by Vansoest et al. (1991) [22]. Mem (Metabolic energy) estimates for growing goats (580 ± 16.5 kJ/kg BW0.75 for dairy goats were greater than that (431 kJ/kg BW0.75) determined by Luo et al. (2004) with regression analysis involving treatment mean observations of heat production or recovered energy [23].

Kids Measurements: Kids' body weights, dam ear number, birth type, gender, and date of birth were recorded at birth, and the kids were housed with their mothers for two weeks following the birth, and then they were housed in a separate compartment created within their main compartment. Starting from the 2nd week, the kids were provided with free kid starter feed and water. Compound feed used in lactation was used as goat growth feed (Table 1). During the 3-month period after birth, live weight, wither height, rump height, rump width, chest width, chest depth, chest circumference and body length measurements of the kids were taken monthly according to the Salako and Ngere method [24].

3. Results and discussion

3.1. Characterization of granulated powder and bolus

The granulation is an important step and intermediate product properties determine not only processing parameters of the tableting process but also the sustained-release properties of a tablet/bolus. Fig. 2a shows a SEM image of the powder mixture of the given formulation. A wide spectrum for particle size of granules (Fig. 2b) with an average particle diameter of around 2 mm was observed in intensity variation vs particle diameter as seen in Fig. 2c [25]. Although spherical shape for granules is expected, different geometries e.g. needle-like structures were also observed. Morphological properties like particle size, shape and distribution, play an important role in sustained-release properties of the bolus [26-27]. Bolus that can range from a weight of 0.5 g to 200 g is a kind of tablet form used for animal applications. In contrast, a weight of tablet forms used in human drug administrations is of relatively small quantities.

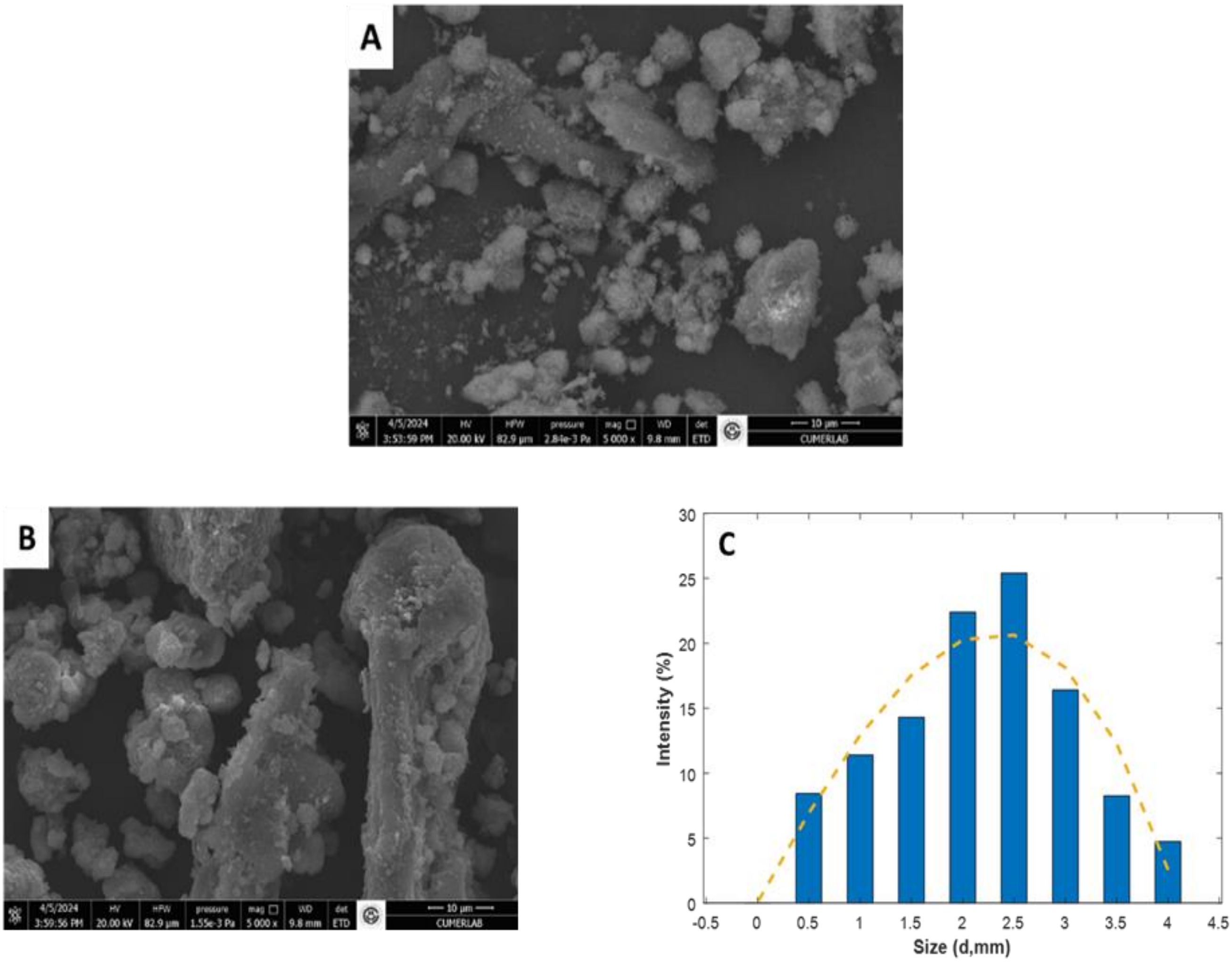

Figure 2. SEM images of the powder without binder (A), the granulated powder with a binder (B) and particle size distribution of granulated powder (C).

Sustained-release boluses may last from minutes (application of bolus in preventing hypocalcemia) to months (application of long term mineral and vitamin support boluses).

3.2. *In vitro* kinetic study and model comparison for dissolution of bolus

The bolus used in the experiment and field studies were of an average weight of 20.2 ± 0.2 g. The suggested release time for boluses with an average of daily release of ~0.17 g/day is given as 120 days. The pump used in the continuous rig, as shown Fig. 1, is a peristaltic pump in which flow rate was calibrated against the speed. The bolus immersed into the beaker was left over time towards a flow rate of 3 mL/min. The immersed bolus was taken out and washed with a deionized water and freeze-dried over a time of 24 hours. The dried bolus was weighted and re-immersed into the beaker in the rig. Fig. 3a shows the cumulative erosion and weight loss of bolus over dissolution time.

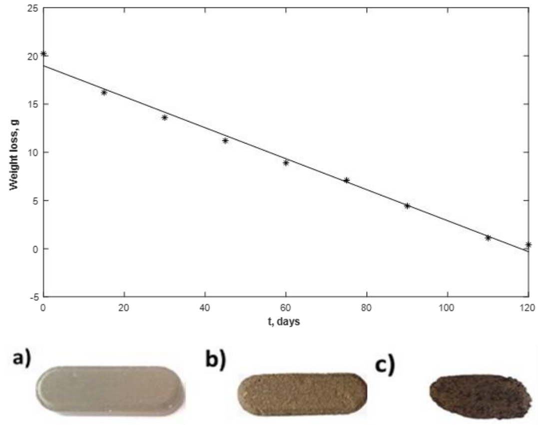

Figure 3. Cumulative release of bolus over time, days: **a)** The fresh bolus before its immersion into artificial saliva, **b)** 10 days after the immersion, **c)** 80 days after the immersion.

The long term sustained-release boluses with a density greater than 2 g/cm³ can remain in the rumen. The addition of powder iron or barium sulphate could be used to increase product density [28]. Composition, pH and temperature of rumen fluid, which are mainly dependent upon feeding type of an animal, microflora of rumen and mechanical contractions occurred within the rumen affect dissolution rate profile of a bolus and therefore release kinetics. The morphological properties of a bolus during its activity in rumen was studied in details by Tefler and Cardinal [26-27]. Fig 3b and c show that there is no crack or deformation but erosion was present over time. This observation may suggest that release mechanism undertakes through surface erosion by linear weight loss and therefore a zero order release kinetic [29].

3.3. *In vivo* performance of sustained-released bolus by Saanen goats

Two groups of 14 Saanen goats were randomly selected and the details (regarding age, milk yield and body weight) about each goat is given as in Table 2.

Table 2. The randomly selected groups of Saanen goats for control (14 animal)and treatment (14 animal).

	Control Group			Treatment Group		
Animal No.	Age Year	Average Milk Yield Kg/day	Body wt. Kg	Age Year	Average Milk Yield Kg/day	Body wt. Kg
1	2	0.70	44.6	5	1.80	62.90
2	5	1.30	53.4	2	1.50	69.30
3	4	1.20	88.4	5	1.80	57.80
4	4	1.50	48.5	5	1.00	74.35
5	5	1.80	70.6	2	1.00	53.00
6	2	1.50	59.0	5	1.50	68.20
7	4	2.70	68.2	2	1.50	65.70
8	4	1.60	67.8	2	2.00	57.00
9	2	1.60	55.1	2	1.30	48.50
10	4	1.70	71.5	4	1.20	52.20
11	4	3.00	60.1	4	1.40	76.60
12	4	2.20	75.4	4	1.40	65.90
13	4	2.30	62.8	4	1.50	73.70
14	4	2.50	79.2	4	1.40	66.70

*These measurements were taken in last three days of the given bolus applied.

Zonturlu (2017) conducted a field study with an addition of vitamin E and trace minerals (Se, Ca, P, Cu, Cu and Co) for Awassi breed sheep that was applied two weeks before the synchronization. The multiple birth rate and fertility rate in their study were reported as 42.9% and 20.0%, respectively, in the treatment group ($P < 0.05$). In our study, a higher rate of multiple births in the treatment group was detected as around 30% of total lambs whereas there was no triplets birth appeared in the control group ($P < 0.05$). The results in the study of Kuru et al. (2020) support these findings of this study as the estrus percentage and multiple pregnancy rates in Pirlak sheep are found to be quantitatively higher and the pregnancy rate was significantly higher [30].

Table 3. Body Weight and Average Rate of Change Comparison of Control and Treatment Groups.

	Single		Twins		Triplets	
	BW. at Birth, kg	RoC of BW	BW. at Birth, kg	RoC of BW	BW. at Birth, kg	RoC of BW
Control	4.32	0.16	3.77	0.12	-	-
Treatment	4.24	0.16	3.83	0.15	3.26	0.13

*BW: Body weight, RoC: Average Rate of Change (kg/day). Number of births as single, twins and triplets for control; 10, 4 and 0, for treatment; 2, 6 and 6, respectively.

As expected, the body weight (BW) at birth decreases from single to triplet births. However, the rate of change in BW significantly increases in twins and triplets ($P<0.05$) compared to control group. This improvement that may be the result of the application of bolus could be related to an improvement in the quality of mother milk. On the contrary, another study reported that Zn, Se and Co as a slow-release ruminal bolus supplement in advanced pregnant Mehraban sheep increased lamb birth weights compared to the treatment group [31]. Abdelrahman et al. (2017) reported that pre-pregnancy slow-release bolus supplements in Najdi sheep improved the blood Co, Zn, Cu, P and Se mineral status of the offspring at birth, increased colostrum quality and increased the birth body weight of the offspring. Zn deficiency can cause abortion in pregnant animals and low birth weight in newborn kids [32].

Table 4. Rate of Change of Development of Rump Width in Control and Treatment Groups.

	RoC for Development of Rump Width (cm/day)		
	Single	Twins	Triplets
Control	0.052	0.047	-
Treatment	0.060	0.056	0.046

In single and twin births, the relative rate of change in rump width is higher at first month however, this RoC significantly declines for both of control and treatment groups in following months.

Table 5. Rate of Change of Chest depth in Control and Treatment Groups.

	RoC for Development of Chest Depth (cm/day)		
	Single	Twins	Triplets
Control	0.081	0.079	-
Treatment	0.103	0.0.095	0.092

For each of single and multiple births there is a distinctive difference between RoC in chest depth of control and treatment groups. Deficiencies in both minerals (e.g I, Cu, Mg, Mn and Se) and vitamins (e.g Vitamin A and E), cause quiescent estrus, anovulation, abortion, and occasionally such births ending up with death [18].

4. Conclusion

The release mechanism and kinetics of sustained-release boluses are of great importance as dissolution and performance of the product are mainly relied on these factors. In this study, the bolus studied had a zero order kinetic based on the surface erosion mechanism. Physical shape of bolus remained relatively constant in comparison to short-term (mins to hours) counterparts. Crack formation throughout the immersion time in artificial saliva was not observed. This linear profile of release kinetic support findings were observed in field trials. The birth rate and ratio of multiple births has significantly increased in treatment groups. In addition, BW at births are relatively higher in similar number of births in treatment group. The administration of bolus to Saanen goats resulted in significant difference for the development of lambs' characteristics such as rump width and chest depth. Countries with high population of small ruminants may benefit from such applications as industrial feeding technologies are barely available in small farms.

Acknowledgements

Authors would like to thank to Çukurova University Faculty of Agriculture Dairy Goat Breeding Research and Application Farm for collecting data and analysis.

Funding

The authors declare that no funds, grants, or other supports were received during the preparation of this manuscript.

Author contributions

Gurbuz Comak: Data curation, Supervision, Validation, Formal analysis, Investigation, Methodology and Writing – original draft. Murat Durmus: Investigation and Methodology: Ibrahim Erez:, Formal analysis, Methodology, Visualization and Writing – review, editing.

Declaration of competing interest

The authors have no relevant financial or non-financial interests to disclose.

Data availability

The authors are unable or have chosen not to specify which data has been used.

References

1. Lawson, D.C., Ritchie, N. S., Parkins, J. J., Hemingway, R. G., & Gresham, H. R. (1990a). Use of a sustained release bolus for enhancing selenium status of cattle. *Veterinary Record*, 127, 67-68.
2. Lawson, D. C., Hemingway, R. G., Parkins, J. J., & Ritchie, N. S. (1990b). Field trials with multi-trace element/vitamin boluses for grazing cattle. *Journal of the Science of Food and Agriculture*, 50, 282-283.
3. Parkins, J. J., Hemingway, R. G., Lawson, D. C., & Ritchie, N. S. (1994). The effectiveness of copper oxide powder as a component of a sustained-release multitrace element and vitamin rumen bolus system for cattle. *British Veterinary Journal*, 150, 547-553.
4. Ruan, X., Gao, X., Gao, Y., Peng, L., Ji, H., Guo, D., & Jiang, S. (2018). Preparation and in vitro release kinetics of ivermectin sustained-release bolus optimized by response surface methodology. *PeerJ*, 6
5. . https://doi.org/10.7717/peerj.5418
6. He, R., Wang, S., Yao, Y., & Wang, Y. (2000). Cu, Co and Se nutritive value of compound trace elements controlled-release boluses for grazing ruminants. *Ying Yong Sheng Tai Xue Bao*, 11, 258-260.
7. Kosgey, I. S., & Okeyo, A. M. (2007). Genetic improvement of small ruminants in low-input, smallholder production systems: Technical and infrastructural issues. *Small Ruminant Research*, 70, 76-88.
8. Sadjadian, R., Seifi, H. A., Mohri, M., Naserian, A. A., & Farzaneh, N. (2013). Variations of energy biochemical metabolites in periparturient dairy Saanen goats. *Comparative Clinical Pathology*, 22, 449–456. https://doi.org/10.1007/s00580-012-1431-8
9. Garcia, A. B., Angeli, N., Machado, L., De Cardoso, F. C., & Gonzalez, F. (2015). Relationships between heat stress and metabolic and milk parameters in dairy cows in Southern Brazil. *Tropical Animal Health and Production*, 47, 889–894. https://doi.org/10.1007/s11250-015-0804-9
10. Kamal, R., Dutt, T., Patel, M., Dey, A., Bharti, P. K., & Chandran, P. C. (2018). Heat stress and effect of shade materials on hormonal and behavior response of dairy cattle: A review. *Tropical Animal Health and Production*, 50, 701–706. https://doi.org/10.1007/s11250-018-1542-6
11. Damarany, A. I., & Ghanem, N. (2020). Effect of flunixine meglumine and aspirin administration on conception rate and estrous cycle characteristics of Egyptian Baladi cows during the hot season. *Tropical Animal Health and Production*, 52, 2969–2976. https://doi.org/10.1007/s11250-020-02314-6
12. Hamzaoui, S., Salama, A. A. K., Albanell, E., Such, X., & Caja, G. (2013). Physiological responses and lactational performances of late-lactation dairy goats under heat stress conditions. *Journal of Dairy Science*, 96, 6355–6365. https://doi.org/10.3168/jds.2013-6665
13. Gwendolyn, L., Carroll, M. S., Matthews, N., Crist, M. A., Thomas, H., & Hartsfield, S. M. (2007). Behavioral, physiological and stress-related hormonal and metabolic responses to intravenous and epidural morphine in goats. *International Journal of Applied Research in Veterinary Medicine*, 5(2), 77-86.
14. Darcan, N., & Güney, O. (2008). Alleviation of climatic stress of dairy goats in the Mediterranean climate. *Small Ruminant Research*, 74, 212-215.
15. Lacetera, N., Bernabucci, U., Ronchi, B., & Nardone, A. (2003). Physiological and productive consequences of heat stress. The case of dairy ruminants. In Lacetera, N., Bernabucci, U., Khalifa, H. H., Ronchi, B., & Nardone, A. (Eds.), *Proceedings of the Symposium on Interaction between Climate and Animal Production: EAAP Technical Series* (No. 7, pp. 45-60).
16. Zarbalizadeh-Saed, A., Seifdavati, J., Abdi-Benemar, H., Salem, A. Z. M., Barbabosa-Pliego, A., Camacho-Diaz, L. M., Fadayifar, A., & Seyed-Sharifi, R. (2020). Effect of slow-release pellets of selenium and iodine on performance and some blood metabolites of pregnant Moghani ewes and their lambs. *Biological Trace Element Research*, 195(2), 461–471. https://doi.org/10.1007/s12011-019-01853
17. Robinson, J. J., Ashworth, C. J., Rooke, J. A., Mitchell, L. M., & McEvoy, T. G. (2006). Nutrition and fertility in ruminant livestock. *Animal Feed Science and Technology*, 126(3-4), 259–276.
18. Kamiloğlu, N. N., Kacar, C., Güven, A., et al. (2017). Changes in lipid peroxidation, glutathione and fertility in Tuj sheep after combined administration of vitamin A and E and passive immunization with testosterone antibodies. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi*, 23(3), 459–465.
19. Smith, M. C., & Sherman, D. M. (2009). *Goat Medicine*. John Wiley & Sons. Vázquez-Armijo, J. F., Rojo, R., López, D., et al. (2011). Trace elements in sheep and goats reproduction: A review. *Tropical and Subtropical Agroecosystems*, 14(1), 1–13.
20. McDougall, E. I. (1948). The composition and output of sheep's saliva. *Biochemical Journal*, 43, 99–109. https://doi.org/10.1042/bj0430099
21. Akan, A. E., & Ünal, F. (2021). An application to error and uncertainty analysis in industrial type dryer experiments. *Turkish Journal of Engineering*, 5(2), 80–86. https://doi.org/10.31127/tuje.679377
22. AOAC. (2005). *Official Methods of Analysis*, 18th ed. Gaithersburg, Maryland, USA: Association of Official Analytical Chemists.
23. Van Soest, P. J., Robertson, J. B., & Lewis, B. A. (1991). Methods for dietary fiber, neutral detergent fiber, and nonstarch polysaccharides in relation to animal nutrition. *Journal of Dairy Science*, 74, 3583-3597.

24. Luo, J., Goetsch, A. L., Nsahlai, I. V., Johnson, Z. B., Sahlu, T., Moore, J. E., Ferrell, C. L., Galyean, M. L., & Owens, F. N. (2004). Maintenance energy needs of goats: Predictions based on observations of heat and recovered energy. *Small Ruminant Research*, 53, 221–230.
25. Salako, A. E., & Ngere, L. O. (2002). Application of multifactorial structural discriminant analysis in the morphometric structural differentiation of West African Dwarf and Yankassa sheep in Southwest Nigeria. *Nigerian Journal of Animal Production*, 29(2), 163–167.
26. Takci, M., Develioğlu, İ., Pulat, H. F., & Demirci, H. E. (2023). Laboratory modeling and analysis of slopes of different geometry under the effect of precipitation. *Turkish Journal of Engineering*, 7(4), 349–357. https://doi.org/10.31127/tuje.1191246
27. Cardinal, J. R. (1985). Controlled drug delivery: Veterinary applications. *Journal of Controlled Release*, 2, 393–403. https://doi.org/10.1016/0168-3659(85)90061-6
28. Telfer, S. B. (1984). Controlled release glass (CRG)—Its action and application in sheep. *Proceedings of the Sheep Veterinary Society*, 8, 82–85.
29. Yelten, A., Öztürk, M. H., & Yılmaz, S. (2022). 3D printing of PLA scaffolds for medical applications. *Turkish Journal of Engineering*, 6(4), 262–267. https://doi.org/10.31127/tuje.958192
30. Hemingway, R. G., Parkins, J. J., & Ritchie, N. S. (1997). Sustained-release boluses to supply trace elements and vitamins to calves. *Veterinary Journal*, 153(2), 221–224.
31. Kuru, M., Kuru, B. B., Sogukpinar, O., et al. (2020). Oestrus synchronisation with progesterone-containing sponge and equine chorionic gonadotropin in Pirlak ewes during the non-breeding season: Can Toryum improve fertility parameters? *Journal of Veterinary Research*, 64(4), 573–579.
32. Aliarabi, H., Fadayifar, A., Alimohamady, R., & Dezfoulian, A. H. (2019). The effect of maternal supplementation of zinc, selenium, and cobalt as slow-release ruminal bolus in late pregnancy on some blood metabolites and performance of ewes and their lambs. *Biological Trace Element Research*, 187, 403–410.
33. Bedwal, R., & Bahuguna, A. (1994). Zinc, copper and selenium in reproduction. *Experientia*, 50, 626–640.

© Author(s) 2024. This work is distributed under https://creativecommons.org/licenses/by-sa/4.0/